STIC Search Report
Biotech-Chem Library

STIC Database Tracking Number: 94933

TO: Josephine Young **Location: 8d04 / 8b19** **Wednesday, June 04, 2003** **Art Unit: 1623** **Phone: 605-1201** **Serial Number: 09 / 844450**	**From: Jan Delaval** **Location: Biotech-Chem Library** **CM1-1E07** **Phone: 308-4498** **jan.delaval@uspto.gov**

Search Notes

Jan Delaval
Reference Librarian
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CM1 1E07 – 703-308-4498
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Jan Delaval
Reference Librarian
Biotechnology & Chemical Library
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=> d his

     (FILE 'HOME' ENTERED AT 08:06:33 ON 04 JUN 2003)
               SET COST OFF

     FILE 'HCAPLUS' ENTERED AT 08:06:47 ON 04 JUN 2003
               E US20020028786/PN
L1             1 S E3
               E WO2001-US13931/AP,PRN
L2             1 S E3,E4
               E US2000-233263/AP,PRN
L3             1 S E5
               E US2000-233025/AP,PRN
L4             1 S E5
               E US2000-230263/AP,PRN
L5             1 S E5
L6             1 S L1-L5
               E HEALTHPARTNER/PA,CS
L7            12 S E5-E11
               E HEALTH PARTNER/PA,CS
L8            23 S (HEALTH(L)PARTN?)/PA,CS
               SEL DN AN 23
L9             1 S L8 AND E1-E3
L10           13 S L7,L9
               E FREY W/AU
L11          167 S E3,E7-E9,E25,E29-E33
               E FAWCETT J/AU
L12           33 S E3,E13
               E FAWCETT JOHN/AU
L13          171 S E3,E6,E7
L14        48821 S ?PYROPHOS?
L15          144 S ?PYRO PHOS?
               E PYROPHOS/CT
               E E16+ALL
L16          851 S E1
               E E2+ALL
L17         8258 S E10+NT
               E E8+ALL
L18        24848 S E4+NT
               E E3+ALL
L19       219974 S E3+NT
L20            2 S L10 AND L14-L19
L21            3 S L11-L13 AND L14-L19
L22            3 S L6,L20,L21
L23            2 S L22 NOT RHODIUM/TI
               E ALZHEIMER/CT
L24        11589 S E3-E20
               E E9+ALL
L25        11603 S E6,E5+NT
L26        11213 S E23+NT OR E24+NT OR E25+NT OR E26+NT OR E27+NT OR E28+NT OR E
               E E23+ALL
L27         1188 S E8
               E E6+ALL
L28        72281 S E7,E6+NT
               E E22+ALL
               E E5+ALL
               E E25+ALL
L29        10751 S E9+NT
               E E8+ALL
L30         2080 S E6,E5+NT
L31        28838 S E15+NT OR E13+NT
               E E10+ALL
               E E27+ALL
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L32          449 S E8-E11
                 E E14+ALL
                 E E28+ALL
                 E E3+ALL
                 E E29+ALL
L33          961 S E3
L34            3 S L10 AND L24-L33
L35           14 S L11-L13 AND L24-L33
L36           14 S L23,L34,L35
L37            4 S L36 AND ?PHOSPH?
L38            2 S L37 AND L23
                 SEL RN

     FILE 'REGISTRY' ENTERED AT 08:21:28 ON 04 JUN 2003
L39           66 S E1-E67
L40           14 S L39 AND P/ELS
L41            3 S L40 AND (C4H8CL3O4P OR C2H8O7P2 OR C3H11NO7P2)
L42            1 S L40 AND H3O3P
L43            2 S L41 AND P>=2
L44           10 S L40 NOT L41,L42
L45           12 S L43,L44
L46          151 S (C6H16O18P4 OR C6H15O15P3 OR C6H14O12P2)/MF AND 46.150.1/RID
L47            9 S 2466-09-3 OR 10380-08-2 OR 13813-62-2 OR 12395-97-0 OR 29444-
L48            1 S 7664-38-2
L49           10 S L47,L48
                 SEL RN
L50       16644 S E68-E77/CRN
L51        2775 S L50 AND PMS/CI
L52         232 S L51 AND HOMOPOLYMER
L53         117 S L52 AND NR>=1
L54         115 S L52 NOT L53
L55          16 S L54 AND (LI OR H3N OR NA)
L56           4 S L55 AND 2/NC
L57           8 S L55 AND 3/NC
L58           1 S L57 AND K
L59           5 S L56,L58
L60        2543 S L51 NOT L52-L59
L61        1751 S L60 AND NR>=1
L62         792 S L60 NOT L61
L63         363 S L62 NOT (C2H4O OR C3H6O)
L64         142 S L63 NOT (N OR S OR SI)/ELS
L65        2697 S L51 AND H3O4P
L66           5 S L65 AND 1/NC
L67           2 S L40 NOT L45
L68           1 S L67 AND H3O3P
L69          22 S L45,L49,L68
L70         170 S L46,L69
L71          10 S (O7P2 OR O13P4 OR O16P5 OR O19P6 OR O22P7 OR O25P8 OR L28P9 O
L72         180 S L70,L71
                 E HEXAMETAPHOSPHATE/CN
L73           1 S E3
L74           2 S E4,E5
                 E OPOP/ES
L75        1511 S (OPOP OR OPOPOP OR OPOPOP OR OPOPOPOP OR OPOPOPOPOP OR OPOPOP
L76         177 S L75 AND 1/NR AND 1/NC
L77         162 S L76 NOT (ETHOXY OR METHOXY OR PROPOXY)
L78         134 S L77 NOT (TIS OR AYS OR MNS)/CI
L79         132 S L78 NOT CCS/CI
L80          50 S L79 NOT (C OR F OR CL OR S OR N)/ELS
L81          41 S L80 NOT RPS/CI
L82          35 S L81 NOT ION
L83           9 S L82 AND (H2O6P2 OR H3O8P3 OR H4O12P4 OR H5O15P5 OR H6O18P6 OR
L84           6 S L83 NOT 3-4/P
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L85           3 S L83 NOT L84
L86           1 S L85 NOT OPOPOP/ES
L87           7 S L84,L86
L88           2 S L75 AND H9O27P9
L89         268 S L75 AND H3O9P3
L90           1 S L89 AND 1/NC
L91           8 S L87,L90
L92         188 S L72,L91
              E GLASS/CN
L93           1 S E56
L94         189 S L92,L93

     FILE 'HCAPLUS' ENTERED AT 09:07:16 ON 04 JUN 2003
L95       81393 S L94
L96        5383 S INOSITOL(L)(DIPHOSPH? OR TRIPHOS? OR TETRAPHOS? OR PENTAPHOS?
L97       82822 S IMIDODIPHOS? OR GUANYLIMIDODIPHOS? OR ADENYLYLIMIDODIPHOS? OR
L98         111 S (ETIDRONIC OR PAMIDRONIC)()ACID

     FILE 'REGISTRY' ENTERED AT 09:08:54 ON 04 JUN 2003

     FILE 'HCAPLUS' ENTERED AT 09:11:24 ON 04 JUN 2003
L99         991 S AMIDRONIC ACID OR (GUANYL? OR ADENYL?)()IMIDODIPHOSPH?
L100     156796 S L95-L98,L99
L101       1483 S L24-L33 AND L100
L102         17 S L10-L13 AND L100
L103          2 S L101 AND L102
L104          2 S L38,L103
L105         15 S L102 NOT L104
L106         91 S L100 (L) THU/RL AND L101
L107         66 S L95 (L) THU/RL AND L106
L108         12 S L107 AND ?ALZHEIM?
L109          9 S L107 AND ?AMYLO?
L110         19 S L108,L109
L111       1277 S L101 AND (PD<=20000501 OR PRD<=20000501 OR AD<=20000501)
L112         63 S L111 AND L106
L113         10 S L110 AND L112
              SEL DN AN 2 3 4 5 6
L114          5 S E1-E15 AND L113
L115         53 S L112 NOT L113
              SEL DN AN 16 28 27 42
L116          4 S E16-E27 AND L115
L117         10 S L114,L116,L104
              SEL HIT RN

    FILE 'REGISTRY' ENTERED AT 09:25:37 ON 04 JUN 2003
L118         16 S E28-E43
L119         15 S L118 NOT UNSPECIFIED

=> fil reg
FILE 'REGISTRY' ENTERED AT 09:26:07 ON 04 JUN 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:     3 JUN 2003  HIGHEST RN 524916-37-8
DICTIONARY FILE UPDATES:    3 JUN 2003  HIGHEST RN 524916-37-8

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2003

  Please note that search-term pricing does apply when
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conducting SmartSELECT searches.

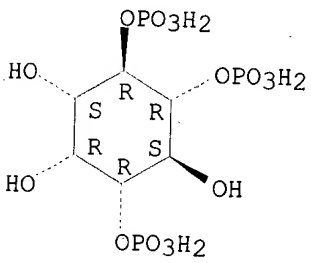
Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=> d ide can tot l119

L119 ANSWER 1 OF 15 REGISTRY COPYRIGHT 2003 ACS
RN **85166-31-0** REGISTRY
CN D-myo-Inositol, 1,4,5-tris(dihydrogen phosphate) (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Inositol triphosphate (6CI, 7CI)
OTHER NAMES:
CN D-myo-Inositol 1,4,5-triphosphate
CN D-myo-Inositol 1,4,5-trisphosphate
CN Inositol trisphosphate
FS STEREOSEARCH
DR 146952-67-2, 346624-32-6
MF C6 H15 O15 P3
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CEN, CHEMCATS, CIN, CSCHEM, EMBASE, MEDLINE, PROMT, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)

Absolute stereochemistry. Rotation (-).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

953 REFERENCES IN FILE CA (1957 TO DATE)
24 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
955 REFERENCES IN FILE CAPLUS (1957 TO DATE)
18 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 138:332173

REFERENCE 2: 138:332169

REFERENCE 3: 138:183487

REFERENCE 4: 138:181193

REFERENCE 5: 138:131350

REFERENCE 6: 138:117878

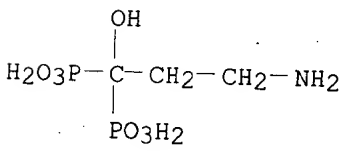
REFERENCE 7: 138:86984

REFERENCE 8: 138:69849

REFERENCE 9: 138:33547

REFERENCE 10: 138:22933

L119 ANSWER 2 OF 15 REGISTRY COPYRIGHT 2003 ACS
RN **40391-99-9** REGISTRY
CN Phosphonic acid, (3-amino-1-hydroxypropylidene)bis- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN (.alpha.-Hydroxy-.gamma.-aminopropylidene)diphosphonic acid
CN (3-Amino-1-hydroxypropylidene)-1,1-bisphosphonate
CN 3-Amino-1-hydroxypropane-1,1-diphosphonic acid
CN 3-Amino-1-hydroxypropylidenediphosphonic acid
CN ADP
CN AHPrBP
CN Amidronic acid
CN Pamidronic acid
CN Propane-1-hydroxy-3-amino-1,1-diphosphonic acid
FS 3D CONCORD
MF C3 H11 N O7 P2
CI COM
LC STN Files: ADISINSIGHT, ADISNEWS, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMINFORMRX, CHEMLIST, CSCHEM, DDFU, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, PHAR, PROMT, SPECINFO, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL, VETU
(*File contains numerically searchable property data)
Other Sources: EINECS**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

640 REFERENCES IN FILE CA (1957 TO DATE)
31 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
646 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 138:352034

REFERENCE 2: 138:348231

REFERENCE 3: 138:331682

REFERENCE 4: 138:331345

REFERENCE 5: 138:326535

REFERENCE 6: 138:326440

REFERENCE 7: 138:297381

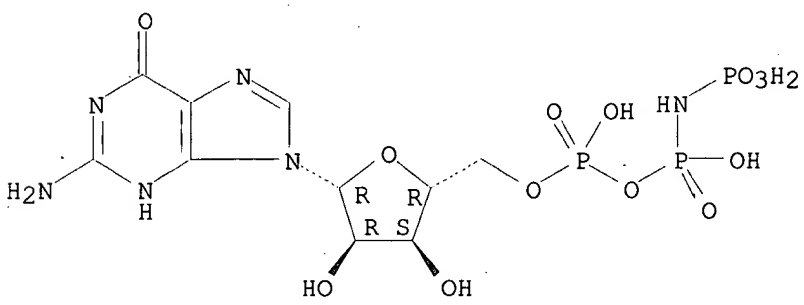
REFERENCE 8: 138:292738

REFERENCE 9: 138:281598

REFERENCE 10: 138:281077

L119 ANSWER 3 OF 15 REGISTRY COPYRIGHT 2003 ACS
RN **34273-04-6** REGISTRY
CN 5'-Guanylic acid, monoanhydride with imidodiphosphoric acid (8CI, 9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Imidodiphosphoric acid, monoanhydride with 5'-guanylic acid (8CI)
OTHER NAMES:
CN .beta.,.gamma.-Imidoguanosine-5'-triphosphate
CN 5'-Guanylyl imidodiphosphate
CN 5'-Guanylyliminodiphosphonate
CN 5-Guanylylimidodiphosphate
CN Guanosine 5'-(.beta.,.gamma.-imido)triphosphate
CN Guanosine 5'-(.beta.,.gamma.-imino)triphosphate
CN Guanylyl imidodiphosphate
CN Guanylyl-.beta.,.gamma.-imidodiphosphate
CN Guanylyl-5'-(.beta.,.gamma.-imido)diphosphate
FS STEREOSEARCH
DR 94725-19-6, 104062-58-0, 104838-92-8, 92836-22-1, 110378-98-8
MF C10 H17 N6 O13 P3
CI COM
LC STN Files: AGRICOLA, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, DDFU, DRUGU, EMBASE, MEDLINE, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2044 REFERENCES IN FILE CA (1957 TO DATE)
47 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
2045 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 138:316710

REFERENCE 2: 138:248790

REFERENCE 3: 138:163487

REFERENCE 4: 138:148027

REFERENCE 5: 138:117741

REFERENCE 6: 137:381427

REFERENCE 7: 137:380285

REFERENCE 8: 137:364731

REFERENCE 9: 137:197091

REFERENCE 10: 137:151462

L119 ANSWER 4 OF 15 REGISTRY COPYRIGHT 2003 ACS
RN **27590-04-1** REGISTRY
CN Imidodiphosphoric acid (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)
OTHER NAMES:
CN Imidobisphosphonic acid
CN Imidodiphosphonic acid
CN Phosphonic acid, iminobis-
FS 3D CONCORD
DR 86960-45-4
MF H5 N O6 P2
CI COM
LC STN Files: BIOSIS, CA, CAOLD, CAPLUS, CHEMLIST, GMELIN*, IFICDB, IFIPAT, IFIUDB, MEDLINE, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)

$H_2O_3P-NH-PO_3H_2$

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

77 REFERENCES IN FILE CA (1957 TO DATE)
16 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
78 REFERENCES IN FILE CAPLUS (1957 TO DATE)
3 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 136:402058

REFERENCE 2: 136:351957

REFERENCE 3: 135:339302

REFERENCE 4: 128:227751

REFERENCE 5: 125:268967

REFERENCE 6: 124:336819

REFERENCE 7: 123:246540

REFERENCE 8: 120:157329

REFERENCE 9: 120:98660

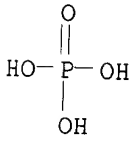
REFERENCE 10: 119:266619

L119 ANSWER 5 OF 15 REGISTRY COPYRIGHT 2003 ACS
RN **27216-57-5** REGISTRY
CN myo-Inositol, bis(dihydrogen phosphate) (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Inositol, bis(dihydrogen phosphate), myo- (8CI)
OTHER NAMES:
CN Inositol bisphosphate

CN Inositol diphosphate
CN myo-Inositol bisphosphate
CN myo-Inositol diphosphate
FS STEREOSEARCH
MF C6 H14 O12 P2
CI IDS
LC STN Files: AGRICOLA, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAPLUS, EMBASE, TOXCENTER, USPATFULL

CM 1

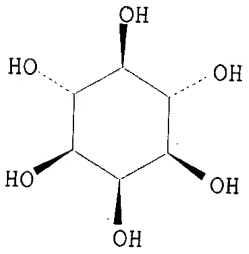
CRN 7664-38-2
CMF H3 O4 P



CM 2

CRN 87-89-8
CMF C6 H12 O6

Relative stereochemistry.



1117 REFERENCES IN FILE CA (1957 TO DATE)
3 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1117 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 138:332173

REFERENCE 2: 138:281373

REFERENCE 3: 138:269332

REFERENCE 4: 137:213385

REFERENCE 5: 136:368759

REFERENCE 6: 136:245048

REFERENCE 7: 135:367189

REFERENCE 8: 135:339302

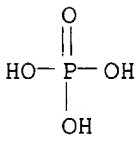
REFERENCE 9: 134:352406

REFERENCE 10: 134:261334

L119 ANSWER 6 OF 15 REGISTRY COPYRIGHT 2003 ACS
RN **27121-72-8** REGISTRY
CN myo-Inositol, tetrakis(dihydrogen phosphate) (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Inositol tetraphosphate (6CI, 7CI)
CN Inositol, tetrakis(dihydrogen phosphate), myo- (8CI)
OTHER NAMES:
CN IP4
CN myo-Inositol tetraphosphate
FS STEREOSEARCH
MF C6 H16 O18 P4
CI IDS, COM
LC STN Files: AGRICOLA, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAOLD, CAPLUS, EMBASE, IFICDB, IFIPAT, IFIUDB, TOXCENTER, USPATFULL

CM 1

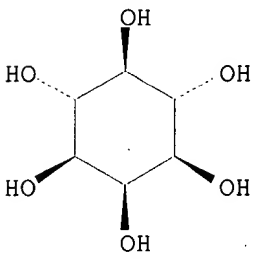
CRN 7664-38-2
CMF H3 O4 P



CM 2

CRN 87-89-8
CMF C6 H12 O6

Relative stereochemistry.



354 REFERENCES IN FILE CA (1957 TO DATE)
9 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
355 REFERENCES IN FILE CAPLUS (1957 TO DATE)
10 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 138:237164

REFERENCE 2: 138:186734

REFERENCE 3: 137:273159

REFERENCE 4: 137:213385

REFERENCE 5: 137:19668

REFERENCE 6: 136:368833

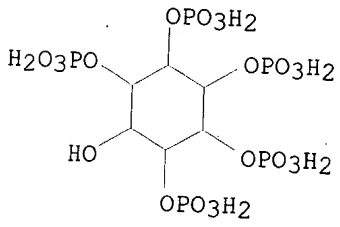
REFERENCE 7: 136:368759

REFERENCE 8: 136:366189

REFERENCE 9: 136:324404

REFERENCE 10: 136:320864

L119 ANSWER 7 OF 15 REGISTRY COPYRIGHT 2003 ACS
RN **25663-09-6** REGISTRY
CN myo-Inositol, pentakis(dihydrogen phosphate) (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Inositol pentaphosphate (7CI)
CN Inositol, pentakis(dihydrogen phosphate), myo- (8CI)
DR 10072-58-9, 53861-65-7, 56688-72-3, 90080-18-5, 27214-04-6
MF C6 H17 O21 P5
CI COM
LC STN Files: AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, EMBASE, MEDLINE, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

244 REFERENCES IN FILE CA (1957 TO DATE)
6 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
245 REFERENCES IN FILE CAPLUS (1957 TO DATE)
6 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 138:270607

REFERENCE 2: 138:249615

REFERENCE 3: 138:237164

REFERENCE 4: 138:13575

REFERENCE 5: 137:278170

REFERENCE 6: 137:262200

REFERENCE 7: 137:213385

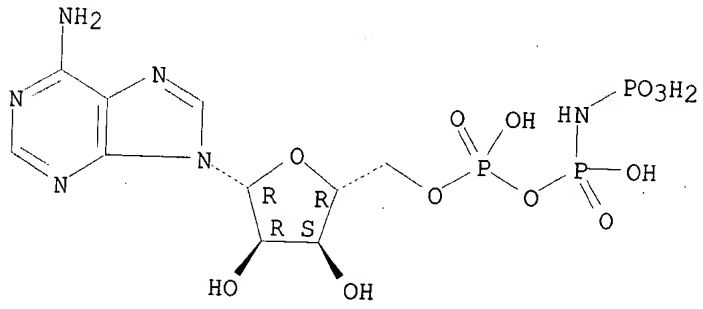
REFERENCE 8: 137:19668

REFERENCE 9: 136:368833

REFERENCE 10: 136:324404

L119 ANSWER 8 OF 15 REGISTRY COPYRIGHT 2003 ACS
RN **25612-73-1** REGISTRY
CN 5'-Adenylic acid, monoanhydride with imidodiphosphoric acid (8CI, 9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Imidodiphosphoric acid, monoanhydride with 5'-adenylic acid (8CI)
OTHER NAMES:
CN .beta.,.gamma.-Imido-ATP
CN .beta.,.gamma.-Imino-adenosine 5'-triphosphate
CN .beta.,.gamma.-Imino-ATP
CN 5'-Adenylyl (.beta.,.gamma.-imidodiphosphate)
CN 5'-Adenylyl imidodiphosphate
CN Adenosine .beta.,.gamma.-imidotriphosphate
CN Adenosine 5'-(.beta.,.gamma.-imidotriphosphate)
CN Adenosine 5'-(.beta.,.gamma.-iminotriphosphate)
CN Adenylyl .beta.,.gamma.-imidodiphosphate
CN Adenylyl imidodiphosphate
CN AMP-PNP
FS STEREOSEARCH
DR 27752-13-2, 33055-51-5
MF C10 H17 N6 O12 P3
CI COM
LC STN Files: AGRICOLA, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, DDFU, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, MEDLINE, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1051 REFERENCES IN FILE CA (1957 TO DATE)
72 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1053 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 138:316772

REFERENCE 2: 138:316723

REFERENCE 3: 138:300376

REFERENCE 4: 138:299471

REFERENCE 5: 138:297992

REFERENCE 6: 138:283198

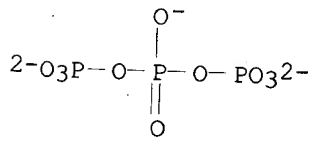
REFERENCE 7: 138:233846

REFERENCE 8: 138:200989

REFERENCE 9: 138:200988

REFERENCE 10: 138:166561

L119 ANSWER 9 OF 15 REGISTRY COPYRIGHT 2003 ACS
RN **14127-68-5** REGISTRY
CN Triphosphate (8CI, 9CI) (CA INDEX NAME)
OTHER NAMES:
CN Triphosphate (P3O105-)
CN Triphosphate(5-)
CN Tripolyphosphate
CN Tripolyphosphate (P3O105-) ion
FS 3D CONCORD
MF O10 P3
CI COM
LC STN Files: ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CEN, CHEMLIST, CIN, EMBASE, GMELIN*, IFICDB, IFIPAT, IFIUDB, IPA, PIRA, PROMT, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**
(**Enter CHEMLIST File for up-to-date regulatory information)



585 REFERENCES IN FILE CA (1957 TO DATE)
17 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
586 REFERENCES IN FILE CAPLUS (1957 TO DATE)

REFERENCE 1: 138:344575

REFERENCE 2: 138:344420

REFERENCE 3: 138:333523

REFERENCE 4: 138:305821

REFERENCE 5: 138:291475

REFERENCE 6: 138:283141

REFERENCE 7: 138:258954

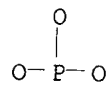
REFERENCE 8: 138:210064

REFERENCE 9: 138:175703

REFERENCE 10: 138:165498

L119 ANSWER 10 OF 15 REGISTRY COPYRIGHT 2003 ACS
RN **13598-36-2** REGISTRY
CN Phosphonic acid (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)
OTHER NAMES:

CN Dihydroxyphosphine oxide
CN Phosphorous acid
MF H3 O3 P
CI COM
LC STN Files: AGRICOLA, ANABSTR, AQUIRE, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, CSNB, DETHERM*, DIPPR*, EMBASE, IFICDB, IFIPAT, IFIUDB, MRCK*, MSDS-OHS, NIOSHTIC, PDLCOM*, PIRA, PROMT, RTECS*, TOXCENTER, TULSA, USPAT2, USPATFULL, VTB
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)



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6229 REFERENCES IN FILE CA (1957 TO DATE)
3012 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
6250 REFERENCES IN FILE CAPLUS (1957 TO DATE)
8 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 138:358492

REFERENCE 2: 138:358405

REFERENCE 3: 138:356459

REFERENCE 4: 138:355998

REFERENCE 5: 138:355997

REFERENCE 6: 138:355994

REFERENCE 7: 138:355117

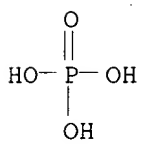
REFERENCE 8: 138:354783

REFERENCE 9: 138:354136

REFERENCE 10: 138:352686

L119 ANSWER 11 OF 15 REGISTRY COPYRIGHT 2003 ACS
RN **7664-38-2** REGISTRY
CN Phosphoric acid (7CI, 8CI, 9CI) (CA INDEX NAME)
OTHER NAMES:
CN 3M Etching Liquid
CN Amberphos 54
CN C 134
CN C 134 (acid)
CN C 434
CN C 434 (acid)
CN Conditioner 36
CN Decon 4512
CN E 338
CN EVITs
CN HQ 54
CN K-etchant
CN Kefo
CN Mikro Klene DF

CN Orthophosphoric acid
CN Panavia Etching Agent
CN Sonac
CN SPA 2
CN SPA 2 (catalyst)
CN TG 434
CN Total Etch
CN Ultra-Etch Gel
CN Ultraetch
CN Uni-Etch
CN WC-Reiniger
FS 3D CONCORD
DR 28602-75-7, 178560-73-1
MF H3 O4 P
CI COM
LC STN Files: AGRICOLA, ANABSTR, AQUIRE, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DETHERM*, DIOGENES, DIPPR*, DRUGU, EMBASE, ENCOMPLIT, ENCOMPLIT2, ENCOMPPAT, ENCOMPPAT2, GMELIN*, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NAPRALERT, NIOSHTIC, PDLCOM*, PIRA, PROMT, RTECS*, SPECINFO, TOXCENTER, TULSA, ULIDAT, USAN, USPAT2, USPATFULL, VETU, VTB
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

52117 REFERENCES IN FILE CA (1957 TO DATE)
7086 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
52174 REFERENCES IN FILE CAPLUS (1957 TO DATE)
1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 138:361751

REFERENCE 2: 138:361709

REFERENCE 3: 138:361656

REFERENCE 4: 138:361639

REFERENCE 5: 138:361638

REFERENCE 6: 138:361419

REFERENCE 7: 138:361300

REFERENCE 8: 138:360392

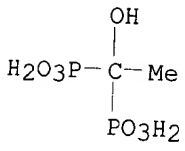
REFERENCE 9: 138:360306

REFERENCE 10: 138:359513

L119 ANSWER 12 OF 15 REGISTRY COPYRIGHT 2003 ACS

RN **2809-21-4** REGISTRY
CN Phosphonic acid, (1-hydroxyethylidene)bis- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Phosphonic acid, (1-hydroxyethylidene)di- (8CI)
OTHER NAMES:
CN (1-Hydroxyethylidene)-1,1-bis(phosphonic acid)
CN (1-Hydroxyethylidene)-1,1-diphosphonic acid
CN (1-Hydroxyethylidene)bisphosphonic acid
CN (1-Hydroxyethylidene)diphosphonic acid
CN 1-Hydroxy-1,1-diphosphonoethane
CN 1-Hydroxyethane-1,1-bisphosphonic acid
CN 1-Hydroxyethane-1,1-diphosphonic acid
CN 1-Hydroxyethane-1,1-diyldiphosphonic acid
CN 1-Hydroxyethanediphosphonic acid
CN 1-Hydroxyethylidene-1,1'-diphosphonic acid
CN 1000SL
CN Acetodiphosphonic acid
CN Anti Cal 5
CN Briquest ADPA 60A
CN Cublen K 60
CN Defloc EH 06
CN Dequest 16
CN Dequest 2010
CN Dequest 2010CS
CN Dequest 2015
CN Dequest Z 010
CN EHDP
CN Ethane-1-hydroxy-1,1-diphosphonic acid
CN Etidronic acid
CN Ferriox 115
CN Ferriox CY 115
CN Ferrofos 510
CN HDEPA
CN HEDP
CN Hydroxyethanediphosphonic acid
CN Ksidifon
CN Lonza 106
CN Mascol P 210
CN Masquol P 210
CN Mayoquest 1500
CN OEDF
CN OEDP
CN Oxyethylidenediphosphonic acid
CN RP 61
CN Sequion 10H
CN Sone 16
CN Tecquest 360
CN Terpil SL
CN Turpinal SL
CN Turpinal SLR
CN Unihib 106
CN Wayplex
CN Xidiphone
CN Xydiphone
FS 3D CONCORD
DR 129130-42-3, 51888-66-5, 66216-98-6, 138360-84-6, 85985-26-8, 86159-18-4, 100511-44-2, 106908-76-3, 192526-55-9, 303177-33-5
MF C2 H8 O7 P2
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMLIST, CIN, CSCHEM, DDFU, DETHERM*, DRUGNL, DRUGU, EMBASE, GMELIN*, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS,

PHAR, PIRA, PROMT, RTECS*, TOXCENTER, USAN, USPAT2, USPATFULL, VETU
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

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433 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
3828 REFERENCES IN FILE CAPLUS (1957 TO DATE)
5 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 138:359460

REFERENCE 2: 138:355337

REFERENCE 3: 138:350529

REFERENCE 4: 138:339805

REFERENCE 5: 138:331682

REFERENCE 6: 138:326535

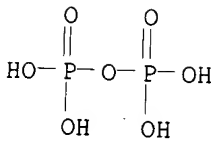
REFERENCE 7: 138:323076

REFERENCE 8: 138:322081

REFERENCE 9: 138:311591

REFERENCE 10: 138:308992

L119 ANSWER 13 OF 15 REGISTRY COPYRIGHT 2003 ACS
RN **2466-09-3** REGISTRY
CN Diphosphoric acid (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Pyrophosphoric acid (8CI)
OTHER NAMES:
CN Diphosphoric acid (H4P2O7)
FS 3D CONCORD
DR 133883-41-7
MF H4 O7 P2
CI COM
LC STN Files: AGRICOLA, BIOBUSINESS, BIOSIS, CA, CAOLD, CAPLUS, CASREACT, CHEMCATS, CHEMLIST, CIN, CSCHEM, DDFU, DETHERM*, DRUGU, EMBASE, GMELIN*, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NIOSHTIC, PIRA, PROMT, RTECS*, TOXCENTER, TULSA, USPAT2, USPATFULL, VTB
(*File contains numerically searchable property data)
Other Sources: EINECS**
(**Enter CHEMLIST File for up-to-date regulatory information)



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2679 REFERENCES IN FILE CA (1957 TO DATE)
583 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
2683 REFERENCES IN FILE CAPLUS (1957 TO DATE)
20 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 138:356235

REFERENCE 2: 138:352686

REFERENCE 3: 138:350389

REFERENCE 4: 138:348010

REFERENCE 5: 138:340726

REFERENCE 6: 138:338001

REFERENCE 7: 138:336931

REFERENCE 8: 138:330038

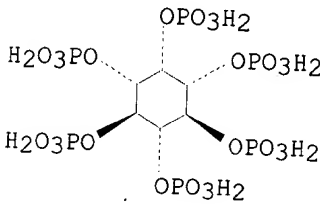
REFERENCE 9: 138:311591

REFERENCE 10: 138:308651

L119 ANSWER 14 OF 15 REGISTRY COPYRIGHT 2003 ACS
RN **83-86-3** REGISTRY
CN myo-Inositol, hexakis(dihydrogen phosphate) (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Inositol, hexakis(dihydrogen phosphate), myo- (8CI)
OTHER NAMES:
CN Alkalovert
CN D-myo-Inositol-1,2,3,4,5,6-hexaphosphate
CN Fytic acid
CN Inositol 1,2,3,4,5,6-hexakisphosphate
CN Inositol hexakis(phosphate)
CN Inositol hexaphosphate
CN IP6
CN meso-Inositol hexaphosphate
CN myo-Inositol hexakis(phosphate)
CN myo-Inositol hexaphosphate
CN Phytic acid
FS STEREOSEARCH
DR 50762-79-3, 78039-41-5
MF C6 H18 O24 P6
CI COM
LC STN Files: AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMLIST, CIN, CSCHEM, DDFU, DRUGU, EMBASE, GMELIN*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NAPRALERT, NIOSHTIC, PHAR, PIRA, PROMT, RTECS*, TOXCENTER, TULSA, USAN, USPAT2, USPATFULL, VETU

(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)

Relative stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

4983 REFERENCES IN FILE CA (1957 TO DATE)
231 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
4996 REFERENCES IN FILE CAPLUS (1957 TO DATE)
5 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 138:356000

REFERENCE 2: 138:353034

REFERENCE 3: 138:339568

REFERENCE 4: 138:336853

REFERENCE 5: 138:336844

REFERENCE 6: 138:336746

REFERENCE 7: 138:336707

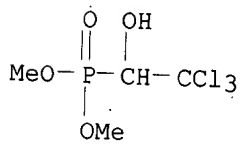
REFERENCE 8: 138:336577

REFERENCE 9: 138:334429

REFERENCE 10: 138:329033

L119 ANSWER 15 OF 15 REGISTRY COPYRIGHT 2003 ACS
RN **52-68-6** REGISTRY
CN Phosphonic acid, (2,2,2-trichloro-1-hydroxyethyl)-, dimethyl ester (6CI, 8CI, 9CI) (CA INDEX NAME)
OTHER NAMES:
CN (.+-.)-Trichlorfon
CN 1-Hydroxy-2,2,2-trichloroethylphosphonate-O,O-dimethyl ester
CN Aerol 1 (pesticide)
CN Agroforotox
CN Anthon
CN BAY-a 9826
CN BAY-L 1359
CN Bayer L 13/59
CN Bayer L 1359
CN Chlorak
CN Chlorofos
CN Chloroftalm
CN Chlorophos
CN Chlorophthalm
CN Chloroxyphos

CN Combot
CN Danex
CN DEP
CN DEP (pesticide)
CN Depthon
CN DETF
CN Dimethyl (2,2,2-trichloro-1-hydroxyethyl)phosphonate
CN Dimethyl 1-hydroxy-2,2,2-trichloroethylphosphonate
CN Dimetox
CN Dioxaphos
CN Dipterex
CN Dipterex 50
CN Dipterex 500
CN Dipterex SL
CN Dipterex WP 80
CN Diptevur
CN Ditrifon
CN Ditriphon 50
CN Dylox
CN Dyrex
CN Dyvon
CN ENT 19,763
CN Flibol E
CN Fliegenteller
CN Forotox
CN Foschlor
CN Foschlor R
CN Foschlor R 50
CN Hypodermacid
CN Loisol
CN Masoten
CN Mazoten
CN Methyl chlorophos
CN Metrifonate
CN Metriphonate
ADDITIONAL NAMES NOT AVAILABLE IN THIS FORMAT - Use FCN, FIDE, or ALL for DISPLAY
FS 3D CONCORD
DR 56042-25-2, 66758-31-4, 50924-44-2, 37333-09-8
MF C4 H8 Cl3 O4 P
CI COM
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, AQUIRE, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DETHERM*, DIOGENES, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NIOSHTIC, PHAR, PHARMASEARCH, PIRA, PROMT, RTECS*, SPECINFO, SYNTHLINE, TOXCENTER, ULIDAT, USAN, USPAT2, USPATFULL, VETU, VTB
(*File contains numerically searchable property data)
Other Sources: EINECS**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

5169 REFERENCES IN FILE CA (1957 TO DATE)
20 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
5171 REFERENCES IN FILE CAPLUS (1957 TO DATE)
297 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 138:333151

REFERENCE 2: 138:299194

REFERENCE 3: 138:297496

REFERENCE 4: 138:287669

REFERENCE 5: 138:286302

REFERENCE 6: 138:282719

REFERENCE 7: 138:281016

REFERENCE 8: 138:267208

REFERENCE 9: 138:267201

REFERENCE 10: 138:251130

=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 09:26:19 ON 04 JUN 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 4 Jun 2003 VOL 138 ISS 23
FILE LAST UPDATED: 3 Jun 2003 (20030603/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d all tot l117

L117 ANSWER 1 OF 10 HCAPLUS COPYRIGHT 2003 ACS
AN 2002:682100 HCAPLUS
TI Inactivation of the human brain muscarinic acetylcholine receptor by oxidative damage catalyzed by a low molecular weight endogenous inhibitor from Alzheimer's brain is prevented by **pyrophosphate** analogs, bioflavonoids and other antioxidants
AU **Fawcett, John R.**; Bordayo, Elizabeth Z.; Jackson, Kathy; Liu, Howard; Peterson, Jennifer; Svitak, Aleta; **Frey, William H., II**
CS The Alzheimer's Research Center, Regions Hospital, **HealthPartners** Research Foundation, St. Paul, MN, 55101-2595, USA
SO Brain Research (2002), 950(1,2), 10-20

CODEN: BRREAP; ISSN: 0006-8993
PB Elsevier Science B.V.
DT Journal
LA English
CC 1-11 (Pharmacology)

AB Oxidative stress has been implicated as a contributing factor to neurodegeneration in Alzheimer's disease. An endogenous, low mol. wt. (LMW) inhibitor from Alzheimer's brain inactivates the human brain muscarinic acetylcholine receptor (mAChR). The inhibitor prevents agonist and antagonist binding to the mAChR as assesssed by radioligand binding studies. The LMW endogenous inhibitor, which has components with mol. wts. between 100 and 1000 Da, requires dissolved oxygen and glutathione. Prevention of inactivation of the mAChR with peroxidase suggests that the LMW endogenous inhibitor generates peroxide. Heme, previously shown to be present in the LMW endogenous inhibitor, also inactivates the mAChR in the presence of peroxide. Free radical damage to the muscarinic receptor by the endogenous inhibitor can be prevented through the use of naturally occurring antioxidants including bilirubin, biliverdin, carnosol, myricetin and quercetin. In addn., **pyrophosphate, imidodiphosphate, bisphosphonates** and related compds. also protect the muscarinic receptor from free radical damage. Inactivation of the mAChR by the LMW endogenous inhibitor is likely to be a factor in the continual decline of Alzheimer's patients, even those taking acetylcholinesterase inhibitors. Natural antioxidants and **pyrophosphate** analogs may improve the effectiveness of acetylcholinesterase inhibitors and prove useful in the treatment and prevention of Alzheimer's disease since the muscarinic acetylcholine receptor is required for memory, and decreased cholinergic function is a crit. deficit in Alzheimer's disease.

ST muscarinic acetylcholine receptor oxidative damage Alzheimer disease **pyrophosphate** analog; neuroprotectant bioflavonoid antioxidant Alzheimer disease **pyrophosphate** analog muscarinic receptor

IT Flavonoids
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bioflavonoids; inactivation of human brain muscarinic acetylcholine receptor by oxidative damage catalyzed by a low mol. wt. endogenous inhibitor from Alzheimer's brain is prevented by **pyrophosphate** analogs, bioflavonoids and other antioxidants)

IT **Anti-Alzheimer's agents**
Brain
Cognition enhancers
Human
Memory, biological
Oxidative stress, biological
(inactivation of human brain muscarinic acetylcholine receptor by oxidative damage catalyzed by a low mol. wt. endogenous inhibitor from Alzheimer's brain is prevented by **pyrophosphate** analogs, bioflavonoids and other antioxidants)

IT Muscarinic receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inactivation of human brain muscarinic acetylcholine receptor by oxidative damage catalyzed by a low mol. wt. endogenous inhibitor from Alzheimer's brain is prevented by **pyrophosphate** analogs, bioflavonoids and other antioxidants)

IT Antioxidants
(natural; inactivation of human brain muscarinic acetylcholine receptor by oxidative damage catalyzed by a low mol. wt. endogenous inhibitor from Alzheimer's brain is prevented by **pyrophosphate** analogs, bioflavonoids and other antioxidants)

IT 114-25-0, Biliverdin 117-39-5, Quercetin 529-44-2, Myricetin 635-65-4, Bilirubin **2466-09-3, Diphosphoric** acid 5957-80-2, Carnosol **14127-68-5, Tripolyphosphate**

25612-73-1 27590-04-1, Imidodiphosphoric acid
34273-04-6 40391-99-9 89771-93-7, Bilirubin ditaurate
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inactivation of human brain muscarinic acetylcholine receptor by oxidative damage catalyzed by a low mol. wt. endogenous inhibitor from Alzheimer's brain is prevented by **pyrophosphate** analogs, bioflavonoids and other antioxidants)

RE.CNT 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
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(17) Hansen, T; Pediatric Res 2001, V49, P203 HCAPLUS
(18) Hortobagyi, G; J Clin Oncol 1998, V16, P2038 MEDLINE
(19) Kanowski, S; Pharmacopsychiatry 1996, V29, P47 MEDLINE
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(21) Khachaturian, Z; Arch Neurol 1985, V42, P1097 MEDLINE
(22) Lander, C; Exp Neurol 1999, V158, P451
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(33) Rhine, W; J Perinatol 2001, V19, P206
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L117 ANSWER 2 OF 10 HCAPLUS COPYRIGHT 2003 ACS
AN **2001:833023** HCAPLUS
DN **135:376738**

TI Compounds and methods for modulating cerebral **amyloid** angiopathy using inhibitors of an **amyloid** .beta. peptide
IN Green, Allan M.; Gervais, Francine
PA Neurochem, Inc., Can.
SO PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001085093	A2	20011115	WO 2000-IB2078	20001222 <--
	WO 2001085093	A3	20020829		
	WO 2001085093	C2	20020926		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 2001084313	A5	20011120	AU 2001-84313	20001222 <--
	EP 1251837	A2	20021030	EP 2000-993855	20001222 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	BR 2000016652	A	20021119	BR 2000-16652	20001222 <--
	US 2003003141	A1	20030102	US 2000-747408	20001222 <--
PRAI	US 1999-171877P	P	19991223 <--		
	WO 2000-IB2078	W	20001222		

OS MARPAT 135:376738
AB The invention provides methods of inhibiting cerebral **amyloid** angiopathy (CAA) and treating a disease state characterized by cerebral **amyloid** angiopathy, e.g., **Alzheimer**'s disease, in a subject using an inhibitor of the 39-40 amino acid **amyloid** .beta. peptide (A.beta.40). The A.beta.40 inhibitor is selected from, e.g., sulfonic acid derivs., such as ethanesulfonic acid, 1,2-ethanedisulfonic acid, 1-propanesulfonic acid, 1,3-propanedisulfonic acid, 1,4-butanedisulfonic acid, 1,5-pentanedisulfonic acid, 2-aminoethanesulfonic acid, 4-hydroxy-1-butanesulfonic acid, 1-butanesulfonic acid, 1-decanesulfonic acid, 2-propanesulfonic acid, 3-pentanesulfonic acid, 4-heptanesulfonic acid, etc., and pharmaceutically acceptable salts thereof or from from phosphonic acid derivs., such as diethylphosphonoacetic acid, phenylphosphonic acid, 3-aminopropylphosphonic acid, propylphosphonic acid, etc. The compds. are formulated in a dispersion system, a liposome formulation, or microspheres using a polymeric matrix. The polymeric matrix is selected from natural polymers, such as albumin, alginate, cellulose derivs., collagen, fibrin, gelatin, and polysaccharides, or synthetic polymers such as polyesters, polyethylene glycol, poloxamers, and polyanhydrides. For example, the ability of compds. of the invention to inhibit CAA was measured in 9 wk old hAPP transgenic mice treated with two different concns. of a compd. of the present invention, 3-amino-1-propanesulfonic acid sodium salt, 100 and 30 mg/kg. Mice were administered the compd. for 8 wk, after which they were sacrificed and their brains were perfused and processed for histol. staining with Thioflavin S. This method may also be used as a screening method for detg. activity of a candidate compd. for inhibiting CAA. The extent of CAA in brain sections obtained from these animals was qual. detd. following staining. The results indicate that the test compd. was

effective in (i) reducing the no. of mice showing CAA, and (ii) showing an effect on the severity of the deposition seen in the brain vasculature of these animals.

ST **amyloid** peptide inhibitor cerebral **amyloid** angiopathy; sulfonate phosphonate **amyloid** peptide inhibitor

IT Brain, disease
(**amyloid** angiopathy; inhibitors of **amyloid** .beta. peptide for modulating cerebral **amyloid** angiopathy)

IT Blood vessel
(endothelium; inhibitors of **amyloid** .beta. peptide for modulating cerebral **amyloid** angiopathy)

IT Brain, disease
(hemorrhagic stroke; inhibitors of **amyloid** .beta. peptide for modulating cerebral **amyloid** angiopathy)

IT **Amyloidosis**
(hereditary, cerebral hemorrhage type, Dutch type; inhibitors of **amyloid** .beta. peptide for modulating cerebral **amyloid** angiopathy)

IT Polyesters, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(hydroxycarboxylic acid-based, matrixes; inhibitors of **amyloid** .beta. peptide for modulating cerebral **amyloid** angiopathy)

IT **Anti-Alzheimer's agents**
Blood vessel
Diagnosis
Imaging agents
Peptidomimetics
(inhibitors of **amyloid** .beta. peptide for modulating cerebral **amyloid** angiopathy)

IT Peptides, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibitors of **amyloid** .beta. peptide for modulating cerebral **amyloid** angiopathy)

IT Lipids, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibitors of **amyloid** .beta. peptide for modulating cerebral **amyloid** angiopathy)

IT Polyesters, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(lactic acid-based, matrixes; inhibitors of **amyloid** .beta. peptide for modulating cerebral **amyloid** angiopathy)

IT Drug delivery systems
(liposomes, multivesicular; inhibitors of **amyloid** .beta. peptide for modulating cerebral **amyloid** angiopathy)

IT Drug delivery systems
(liqs., dispersions; inhibitors of **amyloid** .beta. peptide for modulating cerebral **amyloid** angiopathy)

IT Albumins, biological studies
Biopolymers
Collagens, biological studies
Fibrins
Gelatins, biological studies
Polyanhydrides
Polymers, biological studies
Polyoxyalkylenes, biological studies
Polysaccharides, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(matrixes; inhibitors of **amyloid** .beta. peptide for modulating cerebral **amyloid** angiopathy)

IT Drug delivery systems
(microspheres; inhibitors of **amyloid** .beta. peptide for

modulating cerebral **amyloid** angiopathy)

IT Capillary vessel
(pericyte; inhibitors of **amyloid** .beta. peptide for modulating cerebral **amyloid** angiopathy)

IT Cell death
(prevention of; inhibitors of **amyloid** .beta. peptide for modulating cerebral **amyloid** angiopathy)

IT Muscle
(smooth, blood vessel; inhibitors of **amyloid** .beta. peptide for modulating cerebral **amyloid** angiopathy)

IT Drug delivery systems
(sustained-release; inhibitors of **amyloid** .beta. peptide for modulating cerebral **amyloid** angiopathy)

IT **Amyloid**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(.beta.-; inhibitors of **amyloid** .beta. peptide for modulating cerebral **amyloid** angiopathy)

IT 81-08-3 107-35-7, 2-Aminoethanesulfonic acid 110-04-3, 1,2-Ethanedisulfonic acid 116-63-2 149-45-1 288-94-8, 1H-Tetrazole 594-45-6, Ethanesulfonic acid 831-59-4 860-22-0 926-39-6 993-13-5, Methylphosphonic acid 1068-21-9, Diethyl phosphoramidate 1071-83-6, N-Phosphonomethylglycine 1120-71-4 1132-61-2, 4-Morpholinepropanesulfonic acid 1135-40-6 1571-33-1, Phenylphosphonic acid 1633-83-6 2386-47-2, 1-Butanesulfonic acid 2386-54-1 3095-95-2, Diethylphosphonoacetic acid 3687-18-1, 3-Amino-1-propanesulfonic acid 4408-78-0, Phosphonoacetic acid 4426-50-0 4672-38-2, Propylphosphonic acid 4923-84-6 5117-07-7 5284-66-2, 1-Propanesulfonic acid 5399-58-6 5652-28-8 5994-73-0 6779-09-5, Ethylphosphonic acid 7365-45-9 13138-33-5, 3-Aminopropylphosphonic acid 13419-61-9 13991-98-5 14047-23-5, (1-Aminopropyl)phosphonic acid 14159-48-9, 2-Propanesulfonic acid 14650-46-5 15471-17-7 15763-57-2 18039-42-4 20283-21-0, 1-Decanesulfonic acid 21668-77-9, 1,3-Propanedisulfonic acid 23052-80-4 23052-81-5 25331-57-1 25595-59-9 26978-64-3, 4-Hydroxy-1-butanesulfonic acid 27665-39-0, 1,4-Butanedisulfonic acid 27797-35-9 31465-25-5 34159-44-9 36585-99-6 37810-68-7 38911-09-0 **40391-99-9** 40465-65-4, N-Phosphonomethylglycine trisodium salt 51224-03-4 51224-04-5 51650-30-7, 3-Pentanesulfonic acid 51762-95-9 53329-36-5 57605-13-7 58849-79-9 60142-96-3 63585-09-1, Phosphonoformic acid trisodium salt 71119-22-7 72217-85-7 73858-58-9 75277-39-3 76326-31-3, 2-Amino-5-phosphonopentanoic acid 78739-01-2, D-(-)-2-Amino-4-phosphonobutanoic acid 79055-67-7 79055-68-8 81338-23-0 81338-24-1, L-(+)-2-Amino-7-phosphonoheptanoic acid 82283-67-8 82283-68-9 82977-27-3 87625-44-3 88246-85-9 91357-22-1 91586-81-1 99107-93-4 101020-77-3, 1,5-Pentanedisulfonic acid 102805-84-5 108084-41-9 112980-83-3 117414-74-1 126253-57-4 126453-07-4 128241-72-5 129318-43-0 131177-53-2 138199-51-6 143018-67-1 145544-51-0 157381-42-5 168977-94-4, 3-Aminopropyl(methyl)phosphinic acid hydrochloride 183278-21-9, 4-Heptanesulfonic acid 183278-22-0 183278-30-0 183278-32-2 183278-33-3 183278-34-4 183278-35-5 183278-36-6 183505-70-6 186295-21-6 186295-22-7 188642-79-7 205248-54-0 216367-45-2 216367-47-4 216367-53-2 216367-60-1 216367-67-8 216367-68-9 216367-72-5 216367-73-6 216367-74-7 216367-77-0 216367-78-1 216367-85-0 216367-87-2 216367-89-4 216367-92-9 216367-93-0 216367-94-1 216367-99-6 216368-01-3 216368-05-7 309751-75-5 309751-76-6 309751-77-7 331809-98-4 373644-10-1 373644-12-3 373644-13-4 373644-14-5 373644-15-6 373644-16-7 373644-17-8 373644-18-9 373644-19-0 373644-20-3 373644-21-4 373644-22-5 373644-23-6 373644-24-7 373644-25-8 373644-26-9 373644-27-0 373644-28-1 373644-29-2 373644-30-5 373644-31-6 373644-32-7 373644-33-8 373644-34-9 373644-35-0 373644-36-1 373644-37-2 373644-38-3 373644-39-4 373644-40-7 373644-41-8 373644-42-9

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373645-03-5 373645-04-6 373645-05-7 373645-06-8 373645-07-9
373645-08-0 373645-09-1 373645-10-4 373645-11-5 373645-12-6
373645-13-7 373645-14-8

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(inhibitors of **amyloid** .beta. peptide for modulating cerebral **amyloid** angiopathy)

IT 373645-15-9 373645-16-0 373645-17-1 373645-18-2 373645-19-3
373645-20-6 373645-21-7 373645-22-8 373645-23-9 373645-24-0
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373645-50-2 373645-51-3 373645-52-4 373645-53-5 373645-54-6
373645-56-8 373645-57-9 373645-58-0 373645-59-1 373645-60-4
374078-81-6 374078-82-7

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibitors of **amyloid** .beta. peptide for modulating cerebral **amyloid** angiopathy)

IT 9004-34-6D, Cellulose, ethers, biological studies 9005-32-7, Alginic acid 25322-68-3, Polyethylene glycol 26023-30-3, Poly[oxy(1-methyl-2-oxo-1,2-ethanediyl)] 26100-51-6, Poly(lactic acid) 34346-01-5, Glycolic acid-lactic acid copolymer 106392-12-5, Poloxamer
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(matrixes; inhibitors of **amyloid** .beta. peptide for modulating cerebral **amyloid** angiopathy)

L117 ANSWER 3 OF 10 HCAPLUS COPYRIGHT 2003 ACS
AN **2001:816459** HCAPLUS
DN **135:339302**
TI Methods and compositions for enhancing cellular function through protection of tissue components
IN **Frey, William H., II; Fawcett, John Randall**; Thorne, Robert Gary; Chen, Xueqing
PA **Healthpartners Research Foundation, USA**
SO PCT Int. Appl., 77 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K031-661
ICS A61K031-6615; A61K031-662; A61K031-7084; A61K031-706; A61K031-7076
CC 1-12 (Pharmacology)
Section cross-reference(s): 2, 4, 63
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001082932	A2	20011108	WO 2001-US13931	20010430 <--
	WO 2001082932	A3	20020718		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 2002028786 A1 20020307 US 2001-844450 20010427 <--
EP 1278525 A2 20030129 EP 2001-930957 20010430 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

PRAI US 2000-200843P P 20000501 <--
US 2000-230263P P 20000906 <--
US 2000-233025P P 20000915 <--
US 2000-233263P P 20000918 <--
WO 2001-US13931 W 20010430 <--

OS MARPAT 135:339302

AB Methods and compns. for enhancing cellular function through protection of tissue components, such as receptors, proteins, lipids, nucleic acids, carbohydrates, hormones, vitamins, and cofactors, by administering **pyrophosphate** analogs or related compds. Preferably, the invention provides a method for protecting a muscarinic acetylcholine receptor (mAChR) an/or increasing the efficacy of and agent the directly or indirectly affects a mAChR in a subject in need thereof.

ST tissue component protection **pyrophosphate** analog; cellular function tissue protection **pyrophosphate** analog; muscarinic receptor protection **pyrophosphate** analog

IT Bone, disease
(Paget's, treatment; methods and compns. for enhancing cellular function through protection of tissue components such as muscarinic receptors by administering **pyrophosphate** analogs and combination with other agents)

IT Mental disorder
(affective, treatment; methods and compns. for enhancing cellular function through protection of tissue components such as muscarinic receptors by administering **pyrophosphate** analogs and combination with other agents)

IT Diagnosis
(agents, formulation with **pyrophosphate** derivs. of; methods and compns. for enhancing cellular function through protection of tissue components such as muscarinic receptors by administering **pyrophosphate** analogs and combination with other agents)

IT Nervous system
(amyotrophic lateral sclerosis, treatment; methods and compns. for enhancing cellular function through protection of tissue components such as muscarinic receptors by administering **pyrophosphate** analogs and combination with other agents)

IT Receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(aspartate, protection of; methods and compns. for enhancing cellular function through protection of tissue components such as muscarinic receptors by administering **pyrophosphate** analogs and combination with other agents)

IT Infection
(bacterial, treatment of; methods and compns. for enhancing cellular function through protection of tissue components such as muscarinic receptors by administering **pyrophosphate** analogs and combination with other agents)

IT Gene, animal
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(biliverdin reductase-encoding; methods and compns. for enhancing cellular function through protection of tissue components such as muscarinic receptors by administering **pyrophosphate** analogs and combination with other agents)

IT Flavonoids
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bioflavonoids; methods and compns. for enhancing cellular function through protection of tissue components such as muscarinic receptors by administering **pyrophosphate** analogs and combination with other agents)

IT Neurotrophic factors
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(brain-derived; methods and compns. for enhancing cellular function through protection of tissue components such as muscarinic receptors by administering **pyrophosphate** analogs and combination with other agents)

IT Antitumor agents
(brain; methods and compns. for enhancing cellular function through protection of tissue components such as muscarinic receptors by administering **pyrophosphate** analogs and combination with other agents)

IT Cytoprotective agents
(cardioprotective; methods and compns. for enhancing cellular function through protection of tissue components such as muscarinic receptors by administering **pyrophosphate** analogs and combination with other agents)

IT Gene, animal
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(catalase-encoding; methods and compns. for enhancing cellular function through protection of tissue components such as muscarinic receptors by administering **pyrophosphate** analogs and combination with other agents)

IT Nervous system
(central, disease, from aging, treatment; methods and compns. for enhancing cellular function through protection of tissue components such as muscarinic receptors by administering **pyrophosphate** analogs and combination with other agents)

IT Nervous system
(central, infection, treatment; methods and compns. for enhancing cellular function through protection of tissue components such as muscarinic receptors by administering **pyrophosphate** analogs and combination with other agents)

IT Nervous system
(cerebellar ataxia, treatment; methods and compns. for enhancing cellular function through protection of tissue components such as muscarinic receptors by administering **pyrophosphate** analogs and combination with other agents)

IT Lung, disease
(chronic obstructive, treatment; methods and compns. for enhancing cellular function through protection of tissue components such as muscarinic receptors by administering **pyrophosphate** analogs and combination with other agents)

IT Nucleosides, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES

(Uses)
(di, 5.5'-**pyrophosphate** derivs.; methods and compns. for enhancing cellular function through protection of tissue components such as muscarinic receptors by administering **pyrophosphate** analogs and combination with other agents)

IT Mental disorder
(diffuse Lewy body disease, treatment; methods and compns. for enhancing cellular function through protection of tissue components such as muscarinic receptors by administering **pyrophosphate** analogs and combination with other agents)

IT Esophagus
(disease, achalasia, treatment; methods and compns. for enhancing cellular function through protection of tissue components such as muscarinic receptors by administering **pyrophosphate** analogs and combination with other agents)

IT Spinal cord
(disease, stroke, treatment; methods and compns. for enhancing cellular function through protection of tissue components such as muscarinic receptors by administering **pyrophosphate** analogs and combination with other agents)

IT Blood
Endocrine system
Nervous system
(disease, treatment; methods and compns. for enhancing cellular function through protection of tissue components such as muscarinic receptors by administering **pyrophosphate** analogs and combination with other agents)

IT Intestine, disease
(diverticulitis, treatment; methods and compns. for enhancing cellular function through protection of tissue components such as muscarinic receptors by administering **pyrophosphate** analogs and combination with other agents)

IT Heart, disease
(failure, treatment; methods and compns. for enhancing cellular function through protection of tissue components such as muscarinic receptors by administering **pyrophosphate** analogs and combination with other agents)

IT Poisoning, biological
(from metals, protection from; methods and compns. for enhancing cellular function through protection of tissue components such as muscarinic receptors by administering **pyrophosphate** analogs and combination with other agents)

IT Neurotrophic factors
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(glial-derived; methods and compns. for enhancing cellular function through protection of tissue components such as muscarinic receptors by administering **pyrophosphate** analogs and combination with other agents)

IT Gene, animal
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(heme oxygenase 1- and 2-encoding; methods and compns. for enhancing cellular function through protection of tissue components such as muscarinic receptors by administering **pyrophosphate** analogs and combination with other agents)

IT Proteins, specific or class
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(heme-binding; methods and compns. for enhancing cellular function

through protection of tissue components such as muscarinic receptors by administering **pyrophosphate** analogs and combination with other agents)

IT Hemochromatosis
(hereditary hemochromatosis, treatment; methods and compns. for enhancing cellular function through protection of tissue components such as muscarinic receptors by administering **pyrophosphate** analogs and combination with other agents)

IT Bladder
(incontinence, treatment; methods and compns. for enhancing cellular function through protection of tissue components such as muscarinic receptors by administering **pyrophosphate** analogs and combination with other agents)

IT Heart, disease
(infarction, treatment; methods and compns. for enhancing cellular function through protection of tissue components such as muscarinic receptors by administering **pyrophosphate** analogs and combination with other agents)

IT Animal
Mammal (Mammalia)
Plant (Embryophyta)
(infection in, treatment of; methods and compns. for enhancing cellular function through protection of tissue components such as muscarinic receptors by administering **pyrophosphate** analogs and combination with other agents)

IT Algae
(infection with, treatment of; methods and compns. for enhancing cellular function through protection of tissue components such as muscarinic receptors by administering **pyrophosphate** analogs and combination with other agents)

IT Brain, neoplasm
(inhibitors; methods and compns. for enhancing cellular function through protection of tissue components such as muscarinic receptors by administering **pyrophosphate** analogs and combination with other agents)

IT Intestine, disease
(irritable bowel syndrome, treatment; methods and compns. for enhancing cellular function through protection of tissue components such as muscarinic receptors by administering **pyrophosphate** analogs and combination with other agents)

IT Heart, disease
(ischemia, treatment; methods and compns. for enhancing cellular function through protection of tissue components such as muscarinic receptors by administering **pyrophosphate** analogs and combination with other agents)

IT Carcinogens
(metals, protection from poisoning from; methods and compns. for enhancing cellular function through protection of tissue components such as muscarinic receptors by administering **pyrophosphate** analogs and combination with other agents)

IT **Anti-Alzheimer's agents**
Antiarrhythmics
Antidiabetic agents
Antihypertensives
Antiparkinsonian agents
Antipsychotics
Antitumor agents
Anxiolytics
Cytoprotective agents
Drug interactions
Gene therapy
Genetic vectors
Muscarinic agonists

Muscarinic antagonists
Nervous system agents
(methods and compns. for enhancing cellular function through protection of tissue components such as muscarinic receptors by administering **pyrophosphate** analogs and combination with other agents)

IT Ciliary neurotrophic factor
Gangliosides
Hemopexins
Lipoproteins
Neurokinins
Neurotrophic factors
Phosphatidylserines
Platelet-derived growth factors
Polyphosphates
Thyroid hormones
Transforming growth factors
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods and compns. for enhancing cellular function through protection of tissue components such as muscarinic receptors by administering **pyrophosphate** analogs and combination with other agents)

IT Spinal cord
(neoplasm, inhibitors; methods and compns. for enhancing cellular function through protection of tissue components such as muscarinic receptors by administering **pyrophosphate** analogs and combination with other agents)

IT Plasmid vectors
(nerve growth factor-encoding; methods and compns. for enhancing cellular function through protection of tissue components such as muscarinic receptors by administering **pyrophosphate** analogs and combination with other agents)

IT Gene, animal
mRNA
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nerve growth factor-encoding; methods and compns. for enhancing cellular function through protection of tissue components such as muscarinic receptors by administering **pyrophosphate** analogs and combination with other agents)

IT Nerve, disease
(neuropathy, treatment; methods and compns. for enhancing cellular function through protection of tissue components such as muscarinic receptors by administering **pyrophosphate** analogs and combination with other agents)

IT Cytoprotective agents
(neuroprotectants; methods and compns. for enhancing cellular function through protection of tissue components such as muscarinic receptors by administering **pyrophosphate** analogs and combination with other agents)

IT Proteins, specific or class
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nexins, glial-derived; methods and compns. for enhancing cellular function through protection of tissue components such as muscarinic receptors by administering **pyrophosphate** analogs and combination with other agents)

IT Gene, animal
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(peroxidase-encoding; methods and compns. for enhancing cellular function through protection of tissue components such as muscarinic receptors by administering **pyrophosphate** analogs and combination with other agents)

IT Cations
(protection from poisoning from; methods and compns. for enhancing cellular function through protection of tissue components such as muscarinic receptors by administering **pyrophosphate** analogs and combination with other agents)

IT Metals, biological studies
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(protection from poisoning from; methods and compns. for enhancing cellular function through protection of tissue components such as muscarinic receptors by administering **pyrophosphate** analogs and combination with other agents)

IT Oxidative stress, biological
(protection from; methods and compns. for enhancing cellular function through protection of tissue components such as muscarinic receptors by administering **pyrophosphate** analogs and combination with other agents)

IT 5-HT receptors
Benzodiazepine receptors
Cannabinoid receptors
Carbohydrates, biological studies
Catecholamine receptors
GABA receptors
Glutamate receptors
Glycine receptors
Growth factor receptors
Histamine receptors
Hormones, animal, biological studies
Lipids, biological studies
Muscarinic receptors
Neuropeptide receptors
Neurotransmitter receptors
Neurotrophic factor receptors
Nicotinic receptors
Nucleic acids
Opioid receptors
Proteins, general, biological studies
Purinoceptors
Receptors
Steroid receptors
Vitamins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(protection of; methods and compns. for enhancing cellular function through protection of tissue components such as muscarinic receptors by administering **pyrophosphate** analogs and combination with other agents)

IT Paralysis
(pseudobulbar, treatment; methods and compns. for enhancing cellular function through protection of tissue components such as muscarinic receptors by administering **pyrophosphate** analogs and combination with other agents)

IT Drug delivery systems
(**pyrophosphate** analog-contg.; methods and compns. for enhancing cellular function through protection of tissue components such as muscarinic receptors by administering **pyrophosphate** analogs and combination with other agents)

IT Odor and Odorous substances
(receptors for, protection of; methods and compns. for enhancing cellular function through protection of tissue components such as

muscarinic receptors by administering **pyrophosphate** analogs and combination with other agents)

IT Ion channel
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(receptors for, protection of; methods and compns. for enhancing cellular function through protection of tissue components such as muscarinic receptors by administering **pyrophosphate** analogs and combination with other agents)

IT Muscle, disease
(smooth, treatment; methods and compns. for enhancing cellular function through protection of tissue components such as muscarinic receptors by administering **pyrophosphate** analogs and combination with other agents)

IT Antitumor agents
(spinal cord; methods and compns. for enhancing cellular function through protection of tissue components such as muscarinic receptors by administering **pyrophosphate** analogs and combination with other agents)

IT Brain, disease
Prion diseases
(stroke, treatment; methods and compns. for enhancing cellular function through protection of tissue components such as muscarinic receptors by administering **pyrophosphate** analogs and combination with other agents)

IT Antisense oligonucleotides
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(to nerve growth factors; methods and compns. for enhancing cellular function through protection of tissue components such as muscarinic receptors by administering **pyrophosphate** analogs and combination with other agents)

IT Aging, animal
(treatment of diseases in; methods and compns. for enhancing cellular function through protection of tissue components such as muscarinic receptors by administering **pyrophosphate** analogs and combination with other agents)

IT Mycosis
(treatment of; methods and compns. for enhancing cellular function through protection of tissue components such as muscarinic receptors by administering **pyrophosphate** analogs and combination with other agents),

IT Blood vessel, disease
Bone, disease
Heart, disease
Mental disorder
Multiple sclerosis
Schizophrenia
Sjogren's syndrome
(treatment; methods and compns. for enhancing cellular function through protection of tissue components such as muscarinic receptors by administering **pyrophosphate** analogs and combination with other agents)

IT Mouth
(xerostomia, treatment; methods and compns. for enhancing cellular function through protection of tissue components such as muscarinic receptors by administering **pyrophosphate** analogs and combination with other agents)

IT 9059-22-7, Heme oxygenase
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(1 and 2; methods and compns. for enhancing cellular function through protection of tissue components such as muscarinic receptors by administering **pyrophosphate** analogs and combination with other agents)

IT **13598-36-2D, Phosphonic** acid, alkylidenebis- derivs.
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(**Bisphosphonate**; methods and compns. for enhancing cellular function through protection of tissue components such as muscarinic receptors by administering **pyrophosphate** analogs and combination with other agents)

IT 9001-08-5, Cholinesterase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; methods and compns. for enhancing cellular function through protection of tissue components such as muscarinic receptors by administering **pyrophosphate** analogs and combination with other agents)

IT **52-68-6**, Metrifonate **83-86-3, Inositol hexaphosphate** 114-25-0, Biliverdin 117-39-5, Quercetin 120-73-0D, Purine, **cyclopyrophosphate** analogs 141-43-5, Ethanolamine, biological studies 153-76-4, Gallamine 289-95-2D, Pyrimidine, acyclonucleoside analogs 357-70-0, Galanthamine 529-44-2, Myricetin 635-65-4, Bilirubin, biological studies **2466-09-3, Diphosphoric** acid **2466-09-3D, Diphosphoric** acid, analogs **2809-21-4, Etidronic acid** 5957-80-2, Carnosol 6893-02-3, T3 9001-05-2, Catalase 9003-99-0, Peroxidase 9004-10-8, Insulin, biological studies 9061-61-4, Nerve growth factor 9074-10-6, Biliverdin reductase **14127-68-5, Tripolyphosphate 25612-73-1 25663-09-6, Inositol pentaphosphate 27121-72-8, Inositol tetraphosphate 27216-57-5, Inositol diphosphate 27590-04-1, Imidodiphosphoric** acid **34273-04-6** 37758-47-7, GM-1 ganglioside **40391-99-9, Pamidronic acid** 61912-98-9, Insulin-like growth factor 62031-54-3, Fibroblast growth factor 62229-50-9, Epidermal growth factor 67763-96-6, Insulin-like growth factor 1 67763-97-7, Insulin-like growth factor 2 **85166-31-0, Inositol triphosphate** 106096-92-8, Acidic fibroblast growth factor 106096-93-9, Basic fibroblast growth factor 120014-06-4, Donepezil 123441-03-2, Rivastigmine 130939-66-1, Neurotrophin 3 131986-45-3, Xanomeline 140698-57-3, Activity-dependent neurotrophic factor 143375-33-1, Neurotrophin 4 148499-03-0, Neurotrophin 5
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(methods and compns. for enhancing cellular function through protection of tissue components such as muscarinic receptors by administering **pyrophosphate** analogs and combination with other agents)

IT 7439-89-6, Iron, biological studies 7439-92-1, Lead, biological studies 7439-97-6, Mercury, biological studies 7440-02-0, Nickel, biological studies 7440-38-2, Arsenic, biological studies 7440-43-9, Cadmium, biological studies 7440-47-3, Chromium, biological studies 7440-48-4, Cobalt, biological studies 7440-50-8, Copper, biological studies 7440-62-2, Vanadium, biological studies 14280-50-3, Lead, ion (Pb+2), biological studies 14302-87-5, Mercuric ion, biological studies 15158-11-9, Cupric ion, biological studies 15438-31-0, Ferrous ion, biological studies 22537-48-0, Cadmium, ion (Cd+2), biological studies 22541-54-4, Arsenic, ion (As+3), biological studies
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(protection from poisoning from; methods and compns. for enhancing cellular function through protection of tissue components such as

muscarinic receptors by administering **pyrophosphate** analogs and combination with other agents)

IT 506-32-1, Arachidonic acid 630-08-0, Carbon monoxide, biological studies 10102-43-9, Nitric oxide, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study) (receptors for, protection of; methods and compns. for enhancing cellular function through protection of tissue components such as muscarinic receptors by administering **pyrophosphate** analogs and combination with other agents)

L117 ANSWER 4 OF 10 HCAPLUS COPYRIGHT 2003 ACS
AN **2001:564841** HCAPLUS
DN **135:132470**
TI Selective estrogen receptor modulators in combination with estrogens for therapeutic use
IN Labrie, Fernand
PA Endorecherche, Inc., Can.
SO PCT Int. Appl., 160 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K031-565
ICS A61K031-35; A61P015-12; A61P019-10
CC 1-12 (Pharmacology)
Section cross-reference(s): 2, 27, 63
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001054699	A1	20010802	WO 2001-CA86	20010126 <--
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1251855	A1	20021030	EP 2001-902194	20010126 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	BR 2001008107	A	20030311	BR 2001-8107	20010126 <--
	US 2002198179	A1	20021226	US 2001-52803	20011107 <--
	US 2003040510	A1	20030227	US 2001-52824	20011107 <--
	US 2003065008	A1	20030403	US 2002-143894	20020509 <--
	NO 2002003484	A	20020722	NO 2002-3484	20020722 <--
PRAI	US 2000-178601P	P	20000128	<--	
	US 2001-771180	A1	20010126		
	WO 2001-CA86	W	20010126		

OS MARPAT 135:132470
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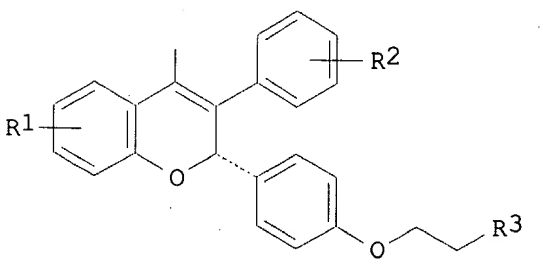

I

AB Methods for redn. or elimination of the incidence of hot flashes and menopausal symptoms, while decreasing the risk of acquiring breast or endometrial cancer and furthermore treating and/or inhibiting the development of osteoporosis, hypercholesterolemia, hyperlipidemia, atherosclerosis, hypertension, insulin resistance, diabetes, loss of muscle mass, obesity, irregular menstruation, **Alzheimer**'s disease, or vaginal dryness in susceptible warm-blooded animals, including humans, involves administration of selective estrogen receptor modulators, particularly compds. I (R1, R2 = OH, moiety convertible to OH in vivo; R3 = (un)satd. (substituted) pyrrolidinyl, (un)satd. (substituted) piperidinyl, etc.) and an amt. of an estrogen or mixed estrogenic/androgenic compd. Further administration of **bisphosphonates**, or a sex steroid precursor is specifically disclosed for the medical treatment and/or inhibition of development of some of these above-mentioned diseases. Pharmaceutical compns. for delivery of active ingredient(s) and kit(s) useful to the invention are also disclosed.

ST therapeutic estrogen receptor modulator estrogen combination; receptor estrogen modulator prepn therapeutic

IT Antiarteriosclerotics
(antiatherosclerotics; selective estrogen receptor modulators in combination with estrogens for therapeutic use)

IT Estrogens
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antiestrogens; selective estrogen receptor modulators in combination with estrogens for therapeutic use)

IT Mammary gland
(breast tenderness from hormone replacement therapy; selective estrogen receptor modulators in combination with estrogens for therapeutic use)

IT Drug delivery systems
(capsules; selective estrogen receptor modulators in combination with estrogens for therapeutic use)

IT Estrogens
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(conjugated; selective estrogen receptor modulators in combination with estrogens for therapeutic use)

IT Bone
(demineralization; selective estrogen receptor modulators in combination with estrogens for therapeutic use)

IT Menopause
(disorder, hot flash, and vasomotor symptoms; selective estrogen receptor modulators in combination with estrogens for therapeutic use)

IT Sleep
(disorder; selective estrogen receptor modulators in combination with estrogens for therapeutic use)

IT Uterus, neoplasm
(endometrium, inhibitors; selective estrogen receptor modulators in combination with estrogens for therapeutic use)

IT Antitumor agents
Uterus
(endometrium; selective estrogen receptor modulators in combination with estrogens for therapeutic use)

IT Uterus
(epithelium; selective estrogen receptor modulators in combination with estrogens for therapeutic use)

IT Menstrual disorder
(irregular menstruation; selective estrogen receptor modulators in

combination with estrogens for therapeutic use)
IT Muscle
(loss of muscle mass; selective estrogen receptor modulators in combination with estrogens for therapeutic use)
IT Antitumor agents
(mammary gland; selective estrogen receptor modulators in combination with estrogens for therapeutic use)
IT Mammary gland
(neoplasm, inhibitors; selective estrogen receptor modulators in combination with estrogens for therapeutic use)
IT Drug delivery systems
(oral; selective estrogen receptor modulators in combination with estrogens for therapeutic use)
IT Estrogens
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phytoestrogens; selective estrogen receptor modulators in combination with estrogens for therapeutic use)
IT Drug delivery systems
(prodrugs; selective estrogen receptor modulators in combination with estrogens for therapeutic use)
IT **Anti-Alzheimer's agents**
Anticholesteremic agents
Antidiabetic agents
Antihypertensives
Antiobesity agents
Drug delivery systems
Drug interactions
Headache
Hypolipemic agents
Menopause
(selective estrogen receptor modulators in combination with estrogens for therapeutic use)
IT Androgens
Estrogens
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(selective estrogen receptor modulators in combination with estrogens for therapeutic use)
IT Estrogen receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(selective estrogen receptor modulators in combination with estrogens for therapeutic use)
IT Osteoporosis
(therapeutic agents; selective estrogen receptor modulators in combination with estrogens for therapeutic use)
IT Hormone replacement therapy
(vaginal bleeding and breast tenderness from; selective estrogen receptor modulators in combination with estrogens for therapeutic use)
IT Vagina
(vaginal bleeding from hormone replacement therapy and vaginal dryness; selective estrogen receptor modulators in combination with estrogens for therapeutic use)
IT 128607-22-7
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Fc 1271; selective estrogen receptor modulators in combination with estrogens for therapeutic use)
IT 130064-21-0P 182167-59-5P 252353-10-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and reaction; selective estrogen receptor modulators in combination with estrogens for therapeutic use)

IT 3144-16-9 17720-60-4 151533-33-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction; selective estrogen receptor modulators in combination with estrogens for therapeutic use)

IT 9004-10-8, Insulin, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(resistance; selective estrogen receptor modulators in combination with estrogens for therapeutic use)

IT 182167-03-9
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(selective estrogen receptor modulators in combination with estrogens for therapeutic use)

IT 13311-84-7, Flutamide
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(selective estrogen receptor modulators in combination with estrogens for therapeutic use)

IT 50-27-1, Estriol 50-27-1D, Estriol, esters 50-28-2, 17.beta.-Estradiol, biological studies 50-28-2D, 17.beta.-Estradiol, esters 53-16-7, Estrone, biological studies 53-16-7D, Estrone, esters 53-43-0, Dehydroepiandrosterone 53-43-0D, Dehydroepiandrosterone, prodrug derivs. 56-53-1, Diethylstilbestrol 57-63-6, 17.alpha.-Ethynylestradiol 57-63-6D, 17.alpha.-Ethynylestradiol, esters 57-91-0, 17.alpha.-Estradiol 57-91-0D, 17.alpha.-Estradiol, esters 58-22-0, Testosterone 58-22-0D, Testosterone, prodrug derivs. 58-72-0D, Triphenylethylene, derivs. 63-05-8, 4-Androstene-3,17-dione 63-05-8D, 4-Androstene-3,17-dione, prodrug derivs. 72-33-3, Mestranol 72-33-3D, Mestranol, esters 85-95-0, Chemestrogen 120-72-9D, Indole, derivs. 254-04-6D, Benzopyran, derivs. 474-86-2, Equilin 474-86-2D, Equilin, esters 521-17-5, Androst-5-ene-3.beta.,17.beta.-diol 521-17-5D, Androst-5-ene-3.beta.,17.beta.-diol, prodrug derivs. 651-48-9, Dehydroepiandrosterone sulfate 651-48-9D, Dehydroepiandrosterone sulfate, prodrug derivs. 5630-53-5, Tibolone 10540-29-1, Tamoxifen 11095-43-5D, Benzothiophene, derivs. **13598-36-2D**, Phosphonic acid, **bisphosphonate** derivs. 16005-17-7, Ethynediol 31477-60-8 31477-60-8D, Centchroman, derivs. 68047-06-3, Hydroxytamoxifen 82413-20-5, Droloxifene 84449-90-1, Raloxifene 89778-26-7, Toremifene 116057-75-1, Idoxifene 151751-78-9, 2'-Ethylestrogenoxazole 155701-61-4, GW5638 175737-59-4, LY 326315 180916-16-9, Lasofoxifene 182133-25-1, LY 353381 198481-33-3, TSE 424 252555-01-4 252555-02-5, EM 1520 252555-03-6, EM 1533 318295-61-3, LY 335563 318295-64-6 318295-65-7 318295-66-8 352233-83-1, HMR 3339 352233-84-2, HMR 3656 352233-85-3, LY 335124 352233-86-4, SH 646 352233-89-7, ERA 923 352233-92-2 352233-93-3 352233-94-4
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(selective estrogen receptor modulators in combination with estrogens for therapeutic use)

IT 57-88-5, Cholesterol, biological studies 9001-78-9, Alkaline phosphatase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(selective estrogen receptor modulators in combination with estrogens for therapeutic use)

RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD

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(1) American Home Prod; EP 0802183 A 1997 HCAPLUS
(2) American Home Prod; WO 9909007 A 1999 HCAPLUS
(3) Behrens, S; WO 0061123 A 2000 HCAPLUS
(4) Couillard, S; JOURNAL OF THE NATIONAL CANCER INSTITUTE 1998, V90(10), P772 HCAPLUS
(5) Deshaies, Y; WO 0101969 A 2001 HCAPLUS
(6) Endorecherche Inc; WO 9963974 A 1999 HCAPLUS
(7) Labrie, F; US 5776923 A 1998 HCAPLUS
(8) Labrie, F; JOURNAL OF STEROID BIOCHEMISTRY AND MOLECULAR BIOLOGY 1999, V69(1 - 06), P51

L117 ANSWER 5 OF 10 HCAPLUS COPYRIGHT 2003 ACS
AN **2001:21335** HCAPLUS
DN **134:91140**
TI Memory-improving compositions containing astaxanthin or its esters
IN Yamashita, Eiji; Hagino, Nobuyoshi
PA Itano Refrigerated Food Co., Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 10 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
IC ICM A61K031-12
ICS A23L001-29; A23L002-52; A61K031-00
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1, 18
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 2001002569	A2	20010109	JP 1999-172757	19990618 <--
PRAI	JP 1999-172757		19990618 <--		

AB The invention provides a memory-improving compn. contg. astaxanthin or its deriv. as a main component. The compn. is suitable for use in a health food. The effect of Astax-1700 contg. astaxanthin esters and polyunsatd. fatty acid triglycerides, on aging-assocd. memory disorder in mouse was examd. Also, tablets were formulated from Astax-1700 5, microcryst. cellulose 20, magnesium stearate 5 g.
ST memory improvement astaxanthin ester
IT Drug delivery systems
(capsules; memory-improving compns. contg. astaxanthin esters)
IT **Memory, biological**
(disorder; memory-improving compns. contg. astaxanthin esters)
IT Beverages
(health; memory-improving compns. contg. astaxanthin esters)
IT Capsules
Feed
Health food
Memory, biological
Tablets
(memory-improving compns. contg. astaxanthin esters)
IT Antioxidants
(memory-improving compns. contg. astaxanthin esters and antioxidants)
IT Flavonoids
Phenols, biological studies
RL: FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(memory-improving compns. contg. astaxanthin esters and antioxidants)
IT Phospholipids, biological studies
RL: FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(memory-improving compns. contg. astaxanthin esters and polyunsatd. fatty acid-contg. glycerides or phospholipids)
IT Candy

Chewing gum
(memory-improving compns. contg. astaxanthin esters for health foods)
IT Glycerides, biological studies
RL: FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polyunsatd. fatty acid-contg.; memory-improving compns. contg. astaxanthin esters and polyunsatd. fatty acid-contg. glycerides or phospholipids)
IT Fatty acids, biological studies
RL: FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polyunsatd., esters; memory-improving compns. contg. astaxanthin esters and polyunsatd. fatty acid-contg. glycerides or phospholipids)
IT Condiments
(rice-seasoning; memory-improving compns. contg. astaxanthin esters for health foods)
IT Drug delivery systems
(tablets; memory-improving compns. contg. astaxanthin esters)
IT 472-61-7, Astaxanthin
RL: FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(memory-improving compns. contg. astaxanthin)
IT 317830-42-5 318235-68-6, Astax 1700
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(memory-improving compns. contg. astaxanthin esters)
IT 50-81-7, Vitamin C, biological studies 70-18-8, Glutathion, biological studies **83-86-3**, Phytic acid 1406-18-4, Vitamin E 7235-40-7, .beta.-Carotene
RL: FFD (Food or feed use); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(memory-improving compns. contg. astaxanthin esters and antioxidants)

L117 ANSWER 6 OF 10 HCAPLUS COPYRIGHT 2003 ACS
AN **2000:481198** HCAPLUS
DN **133:219815**
TI A method for assaying and treating **Alzheimer**'s disease involving **amyloid** precursor protein and heparin or divalent cation
IN Masters, Colin Louis; Bush, Ashley Ian; Beyreuther, Konrad
PA The University of Melbourne, Australia
SO Pat. Specif. (Aust.), 51 pp.
CODEN: ALXXAP
DT Patent
LA English
IC ICM G01N033-573
ICS G01N033-577; C12Q001-68; A61K031-70; A61K031-19; A61K031-44; A61K031-16
CC 9-16 (Biochemical Methods)
Section cross-reference(s): 1, 14
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	AU 701954	B2	19990211	AU 1996-50598	19960410 <--
	AU 9650598	A1	19960711		
PRAI	AU 1996-50598		19960410 <--		

AB The present invention relates to a method of assaying for **Alzheimer**'s disease in a human by detg. the relative abundance of one or more forms of **amyloid** precursor protein (APP) or the enzyme responsible for said forms in circulatory fluid and to a method for treating the disease by modulating divalent cation and/or heparin interaction with APP. Heparin-Sepharose eluates of **Alzheimer**'s disease and control plasma samples were immunoblotted with MAb 22C11 and

the reflectances of the bands at 130, 110, 65 and 42 kDa were measured by computer-assisted image capture anal. The relative amts. of the four APP derivs., as percentages of total lane signal, were detd. in each plasma sample and averaged. The inventors have identified a zinc binding site and a heparin binding site on APP.

ST **Alzheimer** disease treatment diagnosis **amyloid** precursor protein; divalent cation **amyloid** precursor protein **Alzheimer**; zinc heparin **amyloid** precursor protein **Alzheimer**

IT Animal cell line
(PC12, zinc effect on; a method for assaying and treating **Alzheimer**'s disease involving **amyloid** precursor protein and heparin or divalent cation)

IT **Alzheimer's disease**
Blood analysis
(a method for assaying and treating **Alzheimer**'s disease involving **amyloid** precursor protein and heparin or divalent cation)

IT **Amyloid precursor proteins**
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); PUR (Purification or recovery); RCT (Reactant); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); PROC (Process); RACT (Reactant or reagent)
(a method for assaying and treating **Alzheimer**'s disease involving **amyloid** precursor protein and heparin or divalent cation)

IT Blood plasma
Brain
(**amyloid** precursor protein purifn. from, of human; a method for assaying and treating **Alzheimer**'s disease involving **amyloid** precursor protein and heparin or divalent cation)

IT Cations
(divalent; a method for assaying and treating **Alzheimer**'s disease involving **amyloid** precursor protein and heparin or divalent cation)

IT Nervous system
(function of, assessment of; a method for assaying and treating **Alzheimer**'s disease involving **amyloid** precursor protein and heparin or divalent cation)

IT Immunoassay
(immunoblotting; a method for assaying and treating **Alzheimer**'s disease involving **amyloid** precursor protein and heparin or divalent cation)

IT Drug delivery systems
(oral; a method for assaying and treating **Alzheimer**'s disease involving **amyloid** precursor protein and heparin or divalent cation)

IT Nerve
(toxicity; a method for assaying and treating **Alzheimer**'s disease involving **amyloid** precursor protein and heparin or divalent cation)

IT Cations
(trivalent; a method for assaying and treating **Alzheimer**'s disease involving **amyloid** precursor protein and heparin or divalent cation)

IT Biological transport
(uptake, of zinc; a method for assaying and treating **Alzheimer**'s disease involving **amyloid** precursor protein and heparin or divalent cation)

IT 9001-92-7, Protease
RL: ANT (Analyte); ANST (Analytical study)
(APP-degrading; a method for assaying and treating **Alzheimer**

's disease involving **amyloid** precursor protein and heparin or divalent cation)

IT 7440-66-6, Zinc, biological studies 9005-49-6, Heparin, biological studies 23713-49-7, Zinc ion, biological studies
RL: ADV (Adverse effect, including toxicity); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(a method for assaying and treating **Alzheimer**'s disease involving **amyloid** precursor protein and heparin or divalent cation)

IT 7446-70-0, Aluminum chloride, biological studies 7646-85-7, Zinc chloride, biological studies 7733-02-0, Zinc sulfate 7758-89-6, Cuprous chloride 7758-94-3, Ferrous chloride
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(a method for assaying and treating **Alzheimer**'s disease involving **amyloid** precursor protein and heparin or divalent cation)

IT 9005-49-6D, Heparin, conjugates with Sepharose, processes 9012-36-6D, Sepharose, conjugates with heparin
RL: PEP (Physical, engineering or chemical process); PROC (Process)
(**amyloid** precursor protein binding to; a method for assaying and treating **Alzheimer**'s disease involving **amyloid** precursor protein and heparin or divalent cation)

IT 286939-08-0
RL: PEP (Physical, engineering or chemical process); PRP (Properties); PROC (Process)
(as peptide of **amyloid** precursor protein, zinc ion binding to; a method for assaying and treating **Alzheimer**'s disease involving **amyloid** precursor protein and heparin or divalent cation)

IT 60-00-4, EDTA, biological studies 70-51-9, Desferrioxamine **83-86-3**, Phytic acid **83-86-3D**, Phytic acid, derivs. 994-36-5, Sodium citrate 115900-75-9 286014-73-1
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(as zinc binding agent; a method for assaying and treating **Alzheimer**'s disease involving **amyloid** precursor protein and heparin or divalent cation)

IT 149658-70-8
RL: PEP (Physical, engineering or chemical process); PRP (Properties); PROC (Process)
(in characterization of zinc-binding site of **amyloid** precursor protein; a method for assaying and treating **Alzheimer**'s disease involving **amyloid** precursor protein and heparin or divalent cation)

IT 286014-74-2 286014-75-3
RL: PRP (Properties)
(unclaimed sequence; method for assaying and treating **Alzheimer**'s disease involving **amyloid** precursor protein and heparin or divalent cation)

L117 ANSWER 7 OF 10 HCAPLUS COPYRIGHT 2003 ACS
AN **1999:449383** HCAPLUS
DN **131:106661**
TI Solid products containing calcium and phosphate and methods for the remineralization and prevention of demineralization of teeth
IN Winston, Anthony E.; Usen, Norman
PA Enamelon, Inc., USA
SO PCT Int. Appl., 54 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K007-16

ICS A61K007-18
CC 62-7 (Essential Oils and Cosmetics)
Section cross-reference(s): 63
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9934772	A1	19990715	WO 1998-US24529	19981124 <--
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 9915270	A1	19990726	AU 1999-15270	19981124 <--
PRAI	US 1998-5045		19980109 <--		
	WO 1998-US24529		19981124 <--		

AB Solid products for remineralizing dental subsurface lesions and/or mineralizing exposed tubules in dentin contain an anionic component composed of at least one phosphate salt and a cationic component composed of at least one calcium salt. The cationic components and the anionic components are mixed in a carrier component and then coated on an insol., solid substrate. Subsurface lesions and/or exposed dentin tubules in a tooth are remineralized by the rapid and simultaneous release of the calcium and phosphate salts into water and/or saliva such that the subsurface lesions and dentin tubules are permeated by the calcium and phosphate ions. The calcium and phosphate ions ppt. as water-insol. calcium phosphate in the subsurface lesions or dentin tubules. The products may be in the form of dental floss, tooth picks, dental tape, dental adhesives, and implants. E.g., wax-coated nylon 6 fibers were passed through a soln. of the polymeric coating and then the calcium and phosphate salts were dusted onto the wet floss. The floss provides excellent cleaning to the interproximal surfaces of the teeth while delivering an effective amt. of calcium and phosphate salts to remineralize the teeth and to combat dental caries.

ST calcium phosphate dentifrice tooth mineralization; dental adhesive implant floss tooth mineralization

IT Dental materials and appliances
(adhesives; dental solid products contg. calcium and phosphate salts for remineralization and prevention of caries)

IT Saliva
(calcium and phosphate release into; dental solid products contg. calcium and phosphate salts for remineralization and prevention of caries)

IT Tooth
(caries, prevention of; dental solid products contg. calcium and phosphate salts for remineralization and prevention of caries)

IT Dentifrices
(dental floss; dental solid products contg. calcium and phosphate salts for remineralization and prevention of caries)

IT Beeswax
Cotton fibers
Tooth mineralization
Wood
Wool
(dental solid products contg. calcium and phosphate salts for remineralization and prevention of caries)

IT Acetate fibers, biological studies
Paraffin waxes, biological studies
Polyamide fibers, biological studies
Polyamides, biological studies
Polyester fibers, biological studies

Polyoxyalkylenes, biological studies
Polypropene fibers, biological studies
Rayon, biological studies
Waxes
RL: BUU (Biological use, unclassified); DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dental solid products contg. calcium and phosphate salts for remineralization and prevention of caries)

IT Tooth
(dentin; dental solid products contg. calcium and phosphate salts for remineralization and prevention of caries)

IT Tooth
(disease, demineralization, prevention of; dental solid products contg. calcium and phosphate salts for remineralization and prevention of caries)

IT Stabilizing agents
(divalent metal salts; dental solid products contg. calcium and phosphate salts for remineralization and prevention of caries)

IT Ceramics
RL: BUU (Biological use, unclassified); DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(fibers; dental solid products contg. calcium and phosphate salts for remineralization and prevention of caries)

IT Dental materials and appliances
(implants; dental solid products contg. calcium and phosphate salts for remineralization and prevention of caries)

IT Acrylic fibers, biological studies
RL: BUU (Biological use, unclassified); DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methacrylate-based; dental solid products contg. calcium and phosphate salts for remineralization and prevention of caries)

IT Hydrocarbon waxes, biological studies
RL: BUU (Biological use, unclassified); DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(microcryst.; dental solid products contg. calcium and phosphate salts for remineralization and prevention of caries)

IT Dental materials and appliances
(tapes; dental solid products contg. calcium and phosphate salts for remineralization and prevention of caries)

IT Dentifrices
(tooth picks; dental solid products contg. calcium and phosphate salts for remineralization and prevention of caries)

IT 62-54-4, Calcium acetate 64-19-7, Acetic acid, biological studies 77-92-9, biological studies 87-69-4, biological studies 299-28-5, Calcium gluconate 526-95-4, Gluconic acid 814-80-2, Calcium lactate 6915-15-7, Malic acid 7439-95-4D, Magnesium, salts, biological studies 7440-24-6D, Strontium, salts, biological studies 7440-31-5D, Tin, salts, biological studies 7440-66-6D, Zinc, salts, biological studies 7440-70-2D, Calcium, salts, biological studies **7664-38-2**, Phosphoric acid, biological studies **7664-38-2D**, Phosphoric acid, salts, biological studies 7758-23-8, Monocalcium orthophosphate 9000-01-5, Acacia gum 9000-65-1, Gum tragacanth 9003-39-8, Polyvinylpyrrolidone 9004-53-9, Dextrin 9004-64-2, Hydroxypropyl cellulose **9005-25-8**, Starch, biological studies 10043-52-4, Calcium chloride, biological studies 10124-31-9, Ammonium orthophosphate 10124-37-5, Calcium nitrate 16984-48-8, Fluoride, biological studies 25038-54-4, Poly[imino(1-oxo-1,6-hexanediyl)], biological studies 25153-40-6D, Maleic acid-methyl vinyl ether copolymer, alkyl monoesters 25322-68-3 25322-69-4 25609-89-6, Resyn 28-1310 27214-00-2, Calcium glycerophosphate 58748-38-2, Resyn 28-2930 67016-70-0, Amphomer 106392-12-5, Ethylene oxide-propylene oxide block copolymer
RL: BUU (Biological use, unclassified); DEV (Device component use); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)

(dental solid products contg. calcium and phosphate salts for remineralization and prevention of caries)
IT 10103-46-5, Calcium phosphate
RL: FMU (Formation, unclassified); THU (Therapeutic use); BIOL (Biological study); FORM (Formation, nonpreparative); USES (Uses)
(dental solid products contg. calcium and phosphate salts for remineralization and prevention of caries)
RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Constanz; US 5336264 A 1994 HCAPLUS
(2) Curtis; US 5209251 A 1993
(3) Grabenstetter; US 4083955 A 1978
(4) Raaf; US 4397837 A 1983 HCAPLUS
(5) Tung; US 5460803 A 1995 HCAPLUS
(6) Winston; US 5571502 A 1996 HCAPLUS
(7) Winston; US 5614175 A 1997 HCAPLUS
(8) Winston; US 5645853 A 1997 HCAPLUS

L117 ANSWER 8 OF 10 HCAPLUS COPYRIGHT 2003 ACS
AN **1999:422633** HCAPLUS
DN **131:40560**
TI Human chromosome 1p Alzheimer's disease-related gene encodes type 1 **inositol** 1,4,5-**triphosphate** receptor (IP3R1), and use of IP3R1 and its gene (IP3R1) in diagnosis and/or treatment of Alzheimer's disease
IN Belouchi, Magid; Filion, Mario; Fortier, Isabel; Robitaille, Yves; Gauvreau, Denis; Ouellette, Gail
PA Algene Biotechnologies, Can.
SO Can. Pat. Appl., 28 pp.
CODEN: CPXXEB
DT Patent
LA English
IC ICM C12N015-12
ICS A61K048-00; G01N033-566; C12Q001-68; C07K014-705
CC 3-3 (Biochemical Genetics)
Section cross-reference(s): 1, 13, 14
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	CA 2203068	AA	19981018	CA 1997-2203068	19970418 <--
PRAI	CA 1997-2203068		19970418 <--		

AB This invention discloses that the human chromosome 1p Alzheimer's disease (AD)-related gene encodes a member of the **inositol** phosphate pathway, specifically type 1 **inositol** 1,4,5-**triphosphate** receptor (IP3R1). The invention further discloses the use of IP3R1 and its gene (IP3R1) for diagnosis and/or treatment of AD. The invention also described the linkage disequil. mapping used to det. regions of the genome implicated in the physiopathol. of AD.
ST human chromosome 1p **inositol triphosphate** receptor type 1 gene; Alzheimers disease diagnosis treatment human chromosome 1p IP3R1 gene
IT Gene, animal
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(IP3R1; human chromosome 1p Alzheimer's disease-related gene encodes type 1 **inositol** 1,4,5-**triphosphate** receptor (IP3R1), and use of IP3R1 and its gene (IP3R1) in diagnosis and/or treatment of Alzheimer's disease)
IT Chromosome
(human 1, 1p; human chromosome 1p Alzheimer's disease-related gene encodes type 1 **inositol** 1,4,5-**triphosphate** receptor (IP3R1), and use of IP3R1 and its gene (IP3R1) in diagnosis and/or

treatment of Alzheimer's disease)

IT **Alzheimer's disease**
(human chromosome 1p Alzheimer's disease-related gene encodes type 1 **inositol** 1,4,5-**triphosphate** receptor (IP3R1), and use of IP3R1 and its gene (IP3R1) in diagnosis and/or treatment of Alzheimer's disease)

IT Genetic mapping
(linkage; human chromosome 1p Alzheimer's disease-related gene encodes type 1 **inositol** 1,4,5-**triphosphate** receptor (IP3R1), and use of IP3R1 and its gene (IP3R1) in diagnosis and/or treatment of Alzheimer's disease)

IT Diagnosis
(mol.; human chromosome 1p Alzheimer's disease-related gene encodes type 1 **inositol** 1,4,5-**triphosphate** receptor (IP3R1), and use of IP3R1 and its gene (IP3R1) in diagnosis and/or treatment of Alzheimer's disease)

IT **Inositol** 1,4,5-trisphosphate receptors
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(type 1; human chromosome 1p Alzheimer's disease-related gene encodes type 1 **inositol** 1,4,5-**triphosphate** receptor (IP3R1), and use of IP3R1 and its gene (IP3R1) in diagnosis and/or treatment of Alzheimer's disease)

IT 68247-19-8, **Inositol** phosphate
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(pathway; human chromosome 1p Alzheimer's disease-related gene encodes type 1 **inositol** 1,4,5-**triphosphate** receptor (IP3R1), and use of IP3R1 and its gene (IP3R1) in diagnosis and/or treatment of Alzheimer's disease)

L117 ANSWER 9 OF 10 HCAPLUS COPYRIGHT 2003 ACS
AN **1998:394208** HCAPLUS
DN **129:58812**
TI 2-(4-Methoxyphenyl)pyrazolo(4,3-c)quinolin-3-one pharmaceuticals for enhancing cognition
IN Dawson, Gerard Raphael; MacLeod, Angus Murray; Seabrook, Guy Ralph
PA Merck Sharp & Dohme Limited, UK; Dawson, Gerard Raphael; MacLeod, Angus Murray; Seabrook, Guy Ralph
SO PCT Int. Appl., 14 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K031-47
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1, 28
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9824435	A1	19980611	WO 1997-GB3232	19971126 <--
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9851267	A1	19980629	AU 1998-51267	19971126 <--
	AU 731533	B2	20010329		
	EP 956020	A1	19991117	EP 1997-945942	19971126 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
	JP 2001505218	T2	20010417	JP 1998-525315	19971126 <--
	US 6087372	A	20000711	US 1999-308821	19990525 <--
PRAI	GB 1996-25398	A	19961206 <--		

WO 1997-GB3232 W 19971126 <--

AB The present invention provides the use of 2-(4-methoxyphenyl)pyrazolo[4,3-c]quinolin-3-one (I) or its salt for enhancing cognition, particularly in **Alzheimer**'s disease. Thus, I was prepd. by the reaction of Et 4-chloroquinoline-3-carboxylate with 4-methoxyphenylhydrazine-HCl and converted to its (1S)-(+)-10-camphorsulfonate salt (II). A tablet contained II 20, lactose 120, microcryst. cellulose 40, PVP 5, and Mg stearate 5 mg.

ST methoxyphenylpyrazoloquinolinone pharmaceutical cognition enhancer prepn; pyrazoloquinolinone pharmaceutical cognition enhancer prepn

IT **Alzheimer's disease**
Cognition enhancers
((methoxyphenyl)pyrazoloquinolinone pharmaceuticals for enhancing cognition)

IT 13720-94-0 19501-58-7
RL: RCT (Reactant); RACT (Reactant or reagent)
((methoxyphenyl)pyrazoloquinolinone pharmaceuticals for enhancing cognition)

IT 77779-50-1P
RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
((methoxyphenyl)pyrazoloquinolinone pharmaceuticals for enhancing cognition)

IT 50-21-5DP, Lactic acid, (methoxyphenyl)pyrazoloquinolinone pharmaceutical salt 64-19-7DP, Acetic acid, (methoxyphenyl)pyrazoloquinolinone pharmaceutical salt, biological studies 65-85-0DP, Benzoic acid, (methoxyphenyl)pyrazoloquinolinone pharmaceutical salt, biological studies 75-75-2DP, Methanesulfonic acid, (methoxyphenyl)pyrazoloquinolinone pharmaceutical salt 77-92-9DP, Citric acid, (methoxyphenyl)pyrazoloquinolinone pharmaceutical salt 79-09-4DP, Propionic acid, (methoxyphenyl)pyrazoloquinolinone pharmaceutical salt 87-69-4DP, Tartaric acid, (methoxyphenyl)pyrazoloquinolinone pharmaceutical salt, biological studies 110-15-6DP, Succinic acid, (methoxyphenyl)pyrazoloquinolinone pharmaceutical salt 110-16-7DP, Maleic acid, (methoxyphenyl)pyrazoloquinolinone pharmaceutical salt 526-95-4DP, Gluconic acid, (methoxyphenyl)pyrazoloquinolinone pharmaceutical salt 594-45-6DP, Ethanesulfonic acid, (methoxyphenyl)pyrazoloquinolinone pharmaceutical salt 3144-16-9DP, Camphorsulfonic acid, (methoxyphenyl)pyrazoloquinolinone pharmaceutical salt 6915-15-7DP, Malic acid, (methoxyphenyl)pyrazoloquinolinone pharmaceutical salt 7647-01-0DP, Hydrochloric acid, (methoxyphenyl)pyrazoloquinolinone pharmaceutical salt, biological studies **7664-38-2DP**, Phosphoric acid, (methoxyphenyl)pyrazoloquinolinone pharmaceutical salt, biological studies 7664-93-9DP, Sulfuric acid, (methoxyphenyl)pyrazoloquinolinone pharmaceutical salt, biological studies 10035-10-6DP, Hydrobromic acid, (methoxyphenyl)pyrazoloquinolinone pharmaceutical salt, biological studies 77779-50-1DP, salts
RL: SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
((methoxyphenyl)pyrazoloquinolinone pharmaceuticals for enhancing cognition)

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Anon; PHYSIOLOGY AND BEHAVIOR 1987, V41, P241
(2) Bennett, D; US 4595684 A 1986 HCAPLUS
(3) Centre Nat Rech Scient; WO 9221680 A 1992 HCAPLUS
(4) Ciba Geigy Ag; EP 0022078 A 1981 HCAPLUS

L117 ANSWER 10 OF 10 HCAPLUS COPYRIGHT 2003 ACS
AN **1997:717818** HCAPLUS
DN **127:355343**
TI Use of phosphonic acid esters for the treatment of functional disorders of

the brain and depression, and preparation thereof
IN Maurer, Fritz; Schmidt, Bernard; Lensky, Stephan; Van der Staay, Franz-Josef; Fanelli, Richard Joseph; Britelli, David Ross
PA Troponwerke G.m.b.H. & Co. K.-G., Germany; Bayer A.-G.; Maurer, Fritz; Schmidt, Bernard; Lensky, Stephan; Van der Staay, Franz-Josef; Fanelli, Richard Joseph; Britelli, David Ross
SO PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K031-66
ICS C07F009-40; C07M007-00
CC 1-11 (Pharmacology)
Section cross-reference(s): 23, 63
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9739756	A1	19971030	WO 1997-US6469	19970417 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
DE 19616471	A1	19971030	DE 1996-19616471	19960425 <--
AU 9724623	A1	19971112	AU 1997-24623	19970417 <--
EP 896540	A1	19990217	EP 1997-920431	19970417 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, FI, RO				
CN 1222853	A	19990714	CN 1997-195722	19970417 <--
BR 9709300	A	19990810	BR 1997-9300	19970417 <--
JP 2000510455	T2	20000815	JP 1997-538197	19970417 <--
ZA 9703538	A	19971118	ZA 1997-3538	19970424 <--
NO 9804964	A	19981222	NO 1998-4964	19981023 <--
KR 2000010611	A	20000225	KR 1998-708502	19981023 <--
PRAI DE 1996-19616471	A	19960425 <--		
WO 1997-US6469	W	19970417 <--		

OS MARPAT 127:355343
AB Phosphonic acid esters are used for the treatment and prevention of functional disorders of the brain and depression. Some of the compds. of the invention are known; others, e.g. di-Me (1-methanesulfonyloxy-2,2,2-trichloroethane)phosphonate, are prepd. Selected compds. were tested in e.g. a Morris maze test and an active avoidance test.
ST phosphonic acid ester brain functional disorder; depression phosphonic acid ester prepn
IT Mental disorder
(affective; phosphonic acid esters for treatment of brain functional disorders and depression, and prepn. thereof)
IT Amines, miscellaneous
RL: MSC (Miscellaneous)
(basic nitrogen compd. acid-binding agents; phosphonic acid esters for treatment of brain functional disorders and depression, and prepn. thereof)
IT Mental disorder
(cognitive; phosphonic acid esters for treatment of brain functional disorders and depression, and prepn. thereof)
IT **Cognition**
(disorder; phosphonic acid esters for treatment of brain functional disorders and depression, and prepn. thereof)
IT Acids, uses
RL: CAT (Catalyst use); USES (Uses)

(inorg.; phosphonic acid esters for treatment of brain functional disorders and depression, and prepn. thereof)

IT Antidepressants
Brain, disease
Cognition enhancers
Drug delivery systems
Learning
(phosphonic acid esters for treatment of brain functional disorders and depression, and prepn. thereof)

IT Anhydrides
Halogen compounds
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction; phosphonic acid esters for treatment of brain functional disorders and depression, and prepn. thereof)

IT 1554-63-8 10184-66-4 104602-95-1 198561-88-5 198561-89-6
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(isomers; phosphonic acid esters for treatment of brain functional disorders and depression, and prepn. thereof)

IT 198561-90-9P 198561-91-0P 198562-05-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(phosphonic acid esters for treatment of brain functional disorders and depression, and prepn. thereof)

IT 52-68-6 4414-11-3 5952-41-0 10184-68-6 **13598-36-2D,**
Phosphonic acid, esters 61637-95-4 106692-44-8 106692-45-9
198561-92-1 198561-93-2 198561-94-3 198561-95-4 198561-96-5
198561-97-6 198561-98-7 198561-99-8 198562-00-4 198562-01-5
198562-02-6 198562-03-7 198562-04-8 198562-06-0 198562-07-1
198562-08-2 198562-09-3 198562-10-6 198562-11-7 198562-12-8
198562-13-9 198562-14-0 198562-15-1 198562-16-2 198562-17-3
198562-18-4 198562-19-5 198562-20-8 198562-21-9 198562-22-0
198562-23-1 198562-24-2 198562-25-3 198562-26-4 198562-27-5
198562-28-6 198562-29-7 198562-30-0 198562-31-1 198562-32-2
198562-33-3 198562-34-4 198562-35-5 198562-36-6 198562-37-7
198562-38-8 198562-39-9 198562-40-2 198562-42-4 198562-44-6
198562-46-8 198562-50-4 198562-51-5 198562-52-6 198562-53-7
198562-54-8 198562-55-9 198562-56-0 198562-57-1 198562-58-2
198562-59-3
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(phosphonic acid esters for treatment of brain functional disorders and depression, and prepn. thereof)

IT 108-24-7, Acetic anhydride 124-63-0, Methanesulfonic acid chloride 630-19-3, Pivalic aldehyde 868-85-9, Dimethyl phosphite 1538-75-6, Pivalic anhydride
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction; phosphonic acid esters for treatment of brain functional disorders and depression, and prepn. thereof)

=> fil medline
FILE 'MEDLINE' ENTERED AT 09:45:59 ON 04 JUN 2003

FILE LAST UPDATED: 3 JUN 2003 (20030603/UP). FILE COVERS 1958 TO DATE.

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MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2003 vocabulary. See http://www.nlm.nih.gov/mesh/changes2003.html

for a description on changes.

This file contains CAS Registry Numbers for easy and accurate substance identification.

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L143 ANSWER 1 OF 12 MEDLINE
AN 2002470513 MEDLINE
DN 22217278 PubMed ID: 12231224
TI Inactivation of the human brain muscarinic acetylcholine receptor by oxidative damage catalyzed by a low molecular weight endogenous inhibitor from **Alzheimer**'s brain is prevented by pyrophosphate analogs, bioflavonoids and other antioxidants.
AU **Fawcett John R**; Bordayo Elizabeth Z; Jackson Kathy; Liu Howard; Peterson Jennifer; Svitak Aleta; **Frey William H 2nd**
CS The Alzheimer's Research Center, HealthPartners Research Foundation, Regions Hospital, 640 Jackson Street, St. Paul, MN 55101-2595, USA.
SO BRAIN RESEARCH, (2002 Sep 20) 950 (1-2) 10-20.
Journal code: 0045503. ISSN: 0006-8993.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200212
ED Entered STN: 20020917
Last Updated on STN: 20021227
Entered Medline: 20021223
AB Oxidative stress has been implicated as a contributing factor to neurodegeneration in **Alzheimer**'s disease. An endogenous, low molecular weight (LMW) inhibitor from **Alzheimer**'s brain inactivates the human brain muscarinic acetylcholine receptor (mAChR). The inhibitor prevents agonist and antagonist binding to the mAChR as assessed by radioligand binding studies. The LMW endogenous inhibitor, which has components with molecular weights between 100 and 1000 Da, requires dissolved oxygen and glutathione. Prevention of inactivation of the mAChR with peroxidase suggests that the LMW endogenous inhibitor generates peroxide. Heme, previously shown to be present in the LMW endogenous inhibitor, also inactivates the mAChR in the presence of peroxide. Free radical damage to the muscarinic receptor by the endogenous inhibitor can be prevented through the use of naturally occurring antioxidants including bilirubin, biliverdin, carnosol, myricetin and quericetin. In addition, pyrophosphate, **imidodiphosphate**, **bisphosphonates** and related compounds also protect the muscarinic receptor from free radical damage. Inactivation of the mAChR by the LMW endogenous inhibitor is likely to be a factor in the continual decline of **Alzheimer**'s patients, even those taking acetylcholinesterase inhibitors. Natural antioxidants and pyrophosphate analogs may improve the effectiveness of acetylcholinesterase inhibitors and prove useful in the treatment and prevention of **Alzheimer**'s disease since the muscarinic acetylcholine receptor is required for memory, and decreased cholinergic function is a critical deficit in **Alzheimer**'s disease.
CT Check Tags: Human; Support, Non-U.S. Gov't
Alzheimer Disease: DT, drug therapy
***Alzheimer Disease: ME, metabolism**
*Antioxidants: PD, pharmacology
Antioxidants: TU, therapeutic use
*Bioflavonoids: PD, pharmacology
Bioflavonoids: TU, therapeutic use
Brain: DE, drug effects
Brain: ME, metabolism
Catalysis: DE, drug effects

Diphosphates: CH, chemistry
***Diphosphates: PD, pharmacology**
Diphosphates: TU, therapeutic use
Dose-Response Relationship, Drug
*Muscarinic Antagonists: ME, metabolism
Muscarinic Antagonists: PD, pharmacology
*Nerve Tissue Proteins: ME, metabolism
Nerve Tissue Proteins: PD, pharmacology
*Oxidative Stress: DE, drug effects
Oxidative Stress: PH, physiology
*Receptors, Muscarinic: ME, metabolism
CN 0 (Antioxidants); 0 (Bioflavonoids); **0 (Diphosphates)**; 0 (Muscarinic Antagonists); 0 (Nerve Tissue Proteins); 0 (Receptors, Muscarinic); 0 (endogenous modulator protein)

L143 ANSWER 2 OF 12 MEDLINE
AN **1998239725** MEDLINE
DN **98239725** PubMed ID: **9571042**
TI Phosphatidylinositol and inositol involvement in Alzheimer amyloid-beta fibril growth and arrest.
AU McLaurin J; Franklin T; Chakrabartty A; Fraser P E
CS Centre for Research in Neurodegenerative Diseases, University of Toronto, Canada.
SO JOURNAL OF MOLECULAR BIOLOGY, **(1998 Apr 24)** 278 (1) 183-94.
Journal code: 2985088R. ISSN: 0022-2836.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199806
ED Entered STN: 19980708
Last Updated on STN: 19980708
Entered Medline: 19980625
AB A key pathological feature of Alzheimer's disease is the formation and accumulation of amyloid fibres. The major component is the 39 to 42 residue amyloid-beta peptide (Abeta) which is an internal proteolytic fragment of the integral membrane amyloid precursor protein. Aggregation of Abeta into insoluble amyloid fibres is a nucleation-dependent event that may be modulated by the presence of amyloid-associated molecules. Fibril formation is also associated with neurotoxicity which may be the result of specific Abeta interactions with membrane proteins and/or lipids. Using circular dichroism spectroscopy, tyrosine fluorescence spectroscopy and electron microscopy, we have examined the binding of Abeta peptides 1-40 (Abeta40) and 1-42 (Abeta42) to the glycolipid, phosphatidylinositol (PI), and different inositol headgroups. At pH 6.0 and in the presence of PI vesicles, both Abeta40 and Abeta42 adopted an amyloidogenic beta-structure. In contrast, at neutral pH only Abeta42 folded into a beta-structure in the presence of PI vesicles. To determine whether the induction of beta-structure stemmed from interactions with the headgroup of PI, the effects of inositol derivatives on Abeta were also examined. At pH 7.0, myo-inositol was sufficient to induce beta-structure in Abeta42 but had no effect on the conformation of Abeta40. Myo-inositol may promote beta-structure as a result of its ability to be both a hydrogen-bond donor and acceptor. Mono-, di- and triphosphorylated forms of inositol had reduced ability to induce beta-structure in both peptides. The results from this study indicate that interaction of Abeta40 and Abeta42 with PI acts as a seed for fibril formation while myo-inositol stabilizes a soluble Abeta42 micelle.

CT Check Tags: Animal; Support, Non-U.S. Gov't
***Alzheimer Disease: ME, metabolism**
Alzheimer Disease: PA, pathology
Amyloid beta-Protein: AN, analysis

Amyloid beta-Protein: ME, metabolism
Cattle
Inositol: CH, chemistry
*Inositol: ME, metabolism
Inositol 1,4,5-Trisphosphate: ME, metabolism
Inositol Phosphates: ME, metabolism
Peptide Fragments: AN, analysis
Peptide Fragments: ME, metabolism
*Phosphatidylinositols: ME, metabolism
*Protein Conformation
Senile Plaques: ME, metabolism
Senile Plaques: PA, pathology
Time Factors
RN 15421-51-9 (inositol 1-phosphate); **47055-78-7 (inositol 1,4-bis(phosphate))**; 6917-35-7 (Inositol); **85166-31-0 (Inositol 1,4,5-Trisphosphate)**
CN 0 (Amyloid beta-Protein); 0 (Inositol Phosphates); 0 (Peptide Fragments); 0 (Phosphatidylinositols); 0 (amyloid beta-protein (1-40)); 0 (beta-amyloid (1-42))

L143 ANSWER 3 OF 12 MEDLINE
AN **1998166903** MEDLINE
DN **98166903** PubMed ID: **9506003**
TI Prevention and treatment of osteoporosis: does the future belong to hormone replacement therapy?.
AU Gibaldi M
CS Department of Pharmaceutics, School of Pharmacy, University of Washington, Seattle 98195, USA.
SO JOURNAL OF CLINICAL PHARMACOLOGY, **(1997 Dec)** 37 (12) 1087-99.
Ref: 76
Journal code: 0366372. ISSN: 0091-2700.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199803
ED Entered STN: 19980410
Last Updated on STN: 19980410
Entered Medline: 19980330
AB Estrogen replacement therapy (ERT) after menopause prevents the development of osteoporosis and reduces the risk of fracture. Other potential benefits are cardioprotection--probably related to the effects of estrogen on lipid profile and fibrinogen levels--and a delay in the onset of Alzheimer's disease and perhaps amelioration of the disease. ERT, however, increases the risk of endometriosis and endometrial cancer unless given with a progestin for at least 10 days per menstrual cycle. It also results in a small but real increase in breast cancer. Alendronate, a **bisphosphonate**, is the first serious competitor of conjugated equine estrogen for the treatment of osteoporosis. Nearing FDA approval are so-called designer estrogens (e.g., raloxifene), which may selectively prevent osteoporosis with little or no effects on endometrial and breast tissue.
CT Check Tags: Female; Human
*Alendronate: TU, therapeutic use
Alzheimer Disease: PC, prevention & control
Calcitonin: TU, therapeutic use
Calcium: TU, therapeutic use
Coronary Disease: PC, prevention & control
Diphosphonates: TU, therapeutic use
Endometrial Neoplasms: CI, chemically induced
Endometriosis: CI, chemically induced

*Estrogen Replacement Therapy
Estrogen Replacement Therapy: AE, adverse effects
Fluorides, Topical: TU, therapeutic use
Forecasting
*Osteoporosis: DT, drug therapy
*Osteoporosis: PC, prevention & control
Osteoporosis, Postmenopausal: PC, prevention & control
Pulmonary Embolism: CI, chemically induced
Sodium Fluoride: TU, therapeutic use
Thrombosis: CI, chemically induced
Vitamin D: TU, therapeutic use
RN 1406-16-2 (Vitamin D); 66376-36-1 (Alendronate); 7440-70-2 (Calcium); 7681-49-4 (Sodium Fluoride); 9007-12-9 (Calcitonin)
CN 0 (**Diphosphonates**); 0 (Fluorides, Topical)

L143 ANSWER 4 OF 12 MEDLINE
AN **95303354** MEDLINE
DN **95303354** PubMed ID: **7783950**
TI Preservation of acetylcholine muscarinic M2 receptor G-protein interactions in the neocortex of patients with Alzheimer's disease.
AU Hernandez-Hernandez A; Adem A; Ravid R; Cowburn R F
CS Department of Biochemistry and Molecular Biology, University of Salamanca, Spain.
SO NEUROSCIENCE LETTERS, **(1995 Feb 15)** 186 (1) 57-60.
Journal code: 7600130. ISSN: 0304-3940.
CY Ireland
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199507
ED Entered STN: 19950726
Last Updated on STN: 20000303
Entered Medline: 19950714
AB The efficacy of acetylcholine muscarinic M2 receptor-G protein coupling was investigated in Alzheimer's disease and control neocortical membranes by measuring the effects of MgCl2 and 5'-guanylylimidodiphosphate (Gpp[NH]p) on high-affinity [3H]oxotremorine-M ([3H]OXO-M) binding. MgCl2 gave similar enhancements of [3H]OXO-M binding in Alzheimer's disease and control occipital cortex. In contrast, MgCl2 enhanced [3H]OXO-M binding was significantly higher in Alzheimer's disease superior temporal cortex, compared to controls. MgCl2 enhanced [3H]OXO-M binding in both the occipital and temporal cortices of the Alzheimer's disease cases was reversed to control levels by Gpp[NH]p. It is concluded that the number of high-affinity muscarinic M2 sites is increased in Alzheimer's disease superior temporal, but not occipital, cortex and that M2 sites in both regions maintain an efficient G-protein coupling.
CT Check Tags: Female; Human; In Vitro; Male; Support, Non-U.S. Gov't
Aged
***Alzheimer Disease: ME, metabolism**
*Cerebral Cortex: ME, metabolism
*GTP-Binding Proteins: ME, metabolism
Guanylyl Imidodiphosphate: PD, pharmacology
Membranes: ME, metabolism
Muscarinic Antagonists
Oxotremorine: ME, metabolism
*Receptors, Muscarinic: ME, metabolism
RN **34273-04-6 (Guanylyl Imidodiphosphate)**; 70-22-4 (Oxotremorine)
CN 0 (Muscarinic Antagonists); 0 (Receptors, Muscarinic); EC 3.6.1.- (GTP-Binding Proteins)

L143 ANSWER 5 OF 12 MEDLINE
AN **94326289** MEDLINE
DN **94326289** PubMed ID: **7914148**

TI Adenylyl cyclase activity in Alzheimer's disease brain: stimulatory and inhibitory signal transduction pathways are differently affected.

AU Schnecko A; Witte K; Bohl J; Ohm T; Lemmer B
CS Zentrum der Pharmakologie, Johann Wolfgang Goethe-Universitat, Frankfurt, Germany.

SO BRAIN RESEARCH, **(1994 May 2)** 644 (2) 291-6.
Journal code: 0045503. ISSN: 0006-8993.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199409
ED Entered STN: 19940914
Last Updated on STN: 20000303
Entered Medline: 19940908

AB Adenylyl cyclase (AC) activity was studied in post mortem hippocampus and cerebellum from eight patients with Alzheimer's disease/senile dementia of the Alzheimer type (AD/SDAT) and seven non-demented control patients. AC was stimulated via stimulatory guanine nucleotide binding proteins (Gs) using guanosine triphosphate (GTP) and GppNHp (both 10(-4) M) or directly with either forskolin (10(-4) M) or Mn2+ (10(-2) M). Inhibition of AC via A1-receptors was performed with N6-cyclohexyladenosine (CHA) under basal conditions and in the presence of forskolin (10(-5) M). In both brain regions AC activity was significantly reduced in AD/SDAT when compared to controls. Under basal conditions and after stimulation via Gs mean reduction in hippocampus and cerebellum was 47.7% and 58.2%, respectively. The reduction was less pronounced after direct activation of the AC, amounting to 21.8% in hippocampus and 28.1% in cerebellum. CHA inhibited basal and forskolin-stimulated AC concentration-dependently by about 20% (basal) and 30% (forskolin). Inhibition by CHA was similar in hippocampus and cerebellum and tended to be more pronounced in AD/SDAT than in controls. Since the reduction of AC activity in AD/SDAT is greater after stimulation via Gs than after direct activation of the catalytic subunit, we suggest that both Gs and the catalytic subunit seem to be impaired. The fact that CHA-mediated inhibition of AC is not significantly different in AD/SDAT and controls, indicates that in contrast to Gs-, inhibitory G-proteins (Gi) coupling to AC remains intact in Alzheimer's disease.

CT Check Tags: Female; Human; Male; Support, Non-U.S. Gov't
Adenosine: AA, analogs & derivatives
Adenosine: PD, pharmacology
Adenylate Cyclase: AI, antagonists & inhibitors
*Adenylate Cyclase: ME, metabolism
Aged
Aged, 80 and over
***Alzheimer Disease: EN, enzymology**
Alzheimer Disease: PP, physiopathology
Brain: DE, drug effects
Brain: EN, enzymology
Cerebellum: DE, drug effects
Cerebellum: EN, enzymology
Enzyme Activation: DE, drug effects
Forskolin: PD, pharmacology
GTP-Binding Proteins: ME, metabolism
Guanosine Triphosphate: PD, pharmacology
Guanylyl Imidodiphosphate: PD, pharmacology
Hippocampus: DE, drug effects
Hippocampus: EN, enzymology
Manganese: PD, pharmacology
Middle Age
Neurotransmitters: ME, metabolism
Receptors, Purinergic P1: AI, antagonists & inhibitors
*Signal Transduction: PH, physiology
RN **34273-04-6 (Guanylyl Imidodiphosphate)**; 36396-99-3

(N(6)-cyclohexyladenosine); 58-61-7 (Adenosine); 66428-89-5 (Forskolin); 7439-96-5 (Manganese); 86-01-1 (Guanosine Triphosphate)
CN 0 (Neurotransmitters); 0 (Receptors, Purinergic P1); EC 3.6.1.- (GTP-Binding Proteins); EC 4.6.1.1 (Adenylate Cyclase)

L143 ANSWER 6 OF 12 MEDLINE
AN **94230615** MEDLINE
DN **94230615** PubMed ID: **7909814**
TI Kinesin and tau bind to distinct sites on microtubules.
AU Marya P K; Syed Z; Fraylich P E; Eagles P A
CS Department of Molecular Biology and Biophysics, Randall Institute, King's College, University of London, UK.
SO JOURNAL OF CELL SCIENCE, **(1994 Jan)** 107 (Pt 1) 339-44.
Journal code: 0052457. ISSN: 0021-9533.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199406
ED Entered STN: 19940620
Last Updated on STN: 19960312
Entered Medline: 19940606
AB We have used a fluorescent derivative of kinesin, AF-kinesin (kinesin conjugated with 5-(iodoacetamido)fluorescein), to investigate the binding site of kinesin on microtubules and to compare this site with that to which tau binds. Microtubules saturated with tau will bind AF-kinesin in the presence of the ATP analogue, 5'-[beta,gamma-imino]triphosphate (AdoPP[NH]P). This shows that there are distinct binding sites for the two proteins. Further evidence comes from digestion studies where taxol-stabilised microtubules were treated with subtilisin, resulting in the cleavage of C-terminal residues from both the alpha- and beta-tubulin subunits. These treated microtubules can no longer bind tau, but are able to bind AF-kinesin in the presence of AdoPP[NH]P. Finally, AF-kinesin will support the gliding of subtilisin-digested microtubules in the presence of ATP at rates comparable to those obtained with non-digested microtubules. These results show directly that the binding site for kinesin is outside the C-terminal region of tubulin that is removed by subtilisin and is distinct from the binding site of tau.
CT Check Tags: Animal; Support, Non-U.S. Gov't
Adenylyl Imidodiphosphate: PD, pharmacology
Binding Sites
Brain: ME, metabolism
Cattle
Chromatography, DEAE-Cellulose
Chromatography, High Pressure Liquid
Electrophoresis, Polyacrylamide Gel
Fluoresceins
Kinesin: IP, isolation & purification
*Kinesin: ME, metabolism
*Microtubules: ME, metabolism
Microtubules: UL, ultrastructure
Molecular Weight
Paclitaxel: PD, pharmacology
Tubulin: IP, isolation & purification
*Tubulin: ME, metabolism
tau Proteins: IP, isolation & purification
***tau Proteins: ME, metabolism**
RN **25612-73-1 (Adenylyl Imidodiphosphate)**; 33069-62-4 (Paclitaxel); 63368-54-7 (5-iodoacetamidofluorescein)
CN 0 (Fluoresceins); 0 (Tubulin); 0 (tau Proteins); EC 3.6.1.- (Kinesin)

L143 ANSWER 7 OF 12 MEDLINE
AN **92375342** MEDLINE

DN **92375342** PubMed ID: **1508395**
TI Preservation of Gi-protein inhibited adenylyl cyclase activity in the brains of patients with Alzheimer's disease.
AU Cowburn R F; O'Neill C; Ravid R; Winblad B; Fowler C J
CS Department of Geriatric Medicine, Karolinska Institute, Huddinge University Hospital, Sweden.
SO NEUROSCIENCE LETTERS, **(1992 Jul 6)** 141 (1) 16-20.
Journal code: 7600130. ISSN: 0304-3940.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199209
ED Entered STN: 19921009
Last Updated on STN: 20000303
Entered Medline: 19920922
AB The coupling of inhibitory guanine nucleotide binding (Gi) proteins to the adenylyl cyclase signal transduction complex was compared in 4 brain regions from a series of Alzheimer's disease and matched control subjects by measuring the inhibition of membrane enzyme activities in response to guanosine 5'-[beta gamma-imido]**diphosphate** (Gpp[NH]p) and aluminium fluoride (AlF4-). Basal adenylyl cyclase activities were significantly lower in preparations of angular gyrus and frontal and temporal cortices, but not cerebellum, from the Alzheimer's disease cases compared to controls. Gpp[NH]p and AlF4- gave significant inhibitions of adenylyl cyclase activity in all brain regions. The magnitude of these inhibitions, when corrected for altered basal activities, were similar for the Alzheimer's disease and control cases. These results indicate that there is no impairment of Gi-protein mediated inhibition of adenylyl cyclase activity in Alzheimer's disease brain.
CT Check Tags: Human; Support, Non-U.S. Gov't
*Adenylate Cyclase: ME, metabolism
Aluminum: PD, pharmacology
***Alzheimer Disease: EN, enzymology**
*Brain: EN, enzymology
Fluorides: PD, pharmacology
*GTP-Binding Proteins: PH, physiology
Guanylyl Imidodiphosphate: PD, pharmacology
Signal Transduction: PH, physiology
RN **34273-04-6 (Guanylyl Imidodiphosphate)**; 7429-90-5 (Aluminum); 7784-18-1 (aluminum fluoride)
CN 0 (Fluorides); EC 3.6.1.- (GTP-Binding Proteins); EC 4.6.1.1 (Adenylate Cyclase)

L143 ANSWER 8 OF 12 MEDLINE
AN **92177412** MEDLINE
DN **92177412** PubMed ID: **1542114**
TI Metal ion-induced conformational changes of phosphorylated fragments of human neurofilament (NF-M) protein.
AU Hollosi M; Urge L; Perczel A; Kajtar J; Teplan I; Otvos L Jr; Fasman G D
CS Institute of Organic Chemistry, L. Eotvos University, Budapest, Hungary.
NC GM45011 (NIGMS)
SO JOURNAL OF MOLECULAR BIOLOGY, **(1992 Feb 5)** 223 (3) 673-82.
Journal code: 2985088R. ISSN: 0022-2836.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199204
ED Entered STN: 19920424
Last Updated on STN: 19970203
Entered Medline: 19920407
AB The NF-M subunit of human neurofilaments has a C-terminal repeating 13-mer

sequence. The 13-mer (Lys-Ser-Pro-Val-Pro-Lys-Ser-Pro-Val-Glu-Glu-Lys-Gly) (NF-M13) and 17-mer (Glu-Glu-Lys-Gly)-(NF-M13) sequences were synthesized, as were both the mono- and **diphosphorylated** Ser species. Circular dichroism (c.d.) studies and c.d. titrations with Al3+ and Ca2+ were performed. The conformation of the phosphorylated and unphosphorylated material was random in water. Deconvolution of the c.d. spectra, in trifluoroethanol, of the untitrated samples yielded a high content of unordered structure, similar to the poly-L-proline II structure. Titration of the phosphorylated species with Al3+ or Ca2+ caused a surprising conformational change to occur, yielding a high content of beta-pleated sheet structure. A mechanism of metal binding to the phosphofragments is proposed which may be relevant to the formation of neurofibrillary tangles in Alzheimer's disease.

CT Check Tags: Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, Non-P.H.S.; Support, U.S. Gov't, P.H.S.
*Aluminum: CH, chemistry
Amino Acid Sequence
Binding Sites
*Calcium: CH, chemistry
Circular Dichroism
Molecular Sequence Data
***Neurofilament Proteins: CH, chemistry**
Phosphoproteins: CH, chemistry
Phosphorylation
Protein Conformation

RN 111365-29-8 (neurofilament protein M); 7429-90-5 (Aluminum); 7440-70-2 (Calcium)

CN 0 (Neurofilament Proteins); 0 (Phosphoproteins)

L143 ANSWER 9 OF 12 MEDLINE

AN **92168422** MEDLINE

DN **92168422** PubMed ID: **1838799**

TI Preservation of 5-hydroxytryptamine1A receptor-G protein interactions in the cerebral cortex of patients with Alzheimer's disease.

AU O'Neill C; Cowburn R F; Wiehager B; Alafuzoff I; Winblad B; Fowler C J

CS Alzheimer's Disease Research Centre, Karolinska Institute, Department of Geriatric Medicine, Huddinge University Hospital, Sweden.

SO NEUROSCIENCE LETTERS, **(1991 Nov 25)** 133 (1) 15-9.
Journal code: 7600130. ISSN: 0304-3940.

CY Netherlands

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199203

ED Entered STN: 19920417
Last Updated on STN: 20000303
Entered Medline: 19920331

AB The coupling of 5-hydroxytryptamine1A (5-HT1A) receptors to guanine nucleotide binding (G) proteins was investigated in membranes prepared from frontal and parietal cortices of control and Alzheimer's disease brains by characterising the effect of guanosine 5'-[beta gamma-imido] **diphosphate** (Gpp[NH]p) on [3H]8-hydroxy-2-(di-n-propylamino)-tetralin ([3H]8-OH-DPAT) binding parameters. In the absence of guanine nucleotides, [3H]8-OH-DPAT bound to a single high affinity binding site in all membrane types. The number of [3H]8-OH-DPAT binding sites was significantly decreased in the parietal cortex of Alzheimer's disease samples compared with controls, whereas in the frontal cortex the number of binding sites remained unchanged. Gpp[NH]p reduced the [3H]8-OH-DPAT binding affinity and the number of binding sites to the same degree in both regions in control and Alzheimer's disease cases. [3H]8-OH-DPAT binding was inhibited in a concentration dependent manner with an IC50 value of approximately 1 microM in all cases. These results suggest that the 5-HT1A receptor-G protein complex is functionally intact in these

regions in Alzheimer's disease brain.
CT Check Tags: Female; Human; In Vitro; Male; Support, Non-U.S. Gov't
8-Hydroxy-2-(di-n-propylamino)tetralin
Aged
***Alzheimer Disease: ME, metabolism**
Cerebral Cortex: DE, drug effects
*Cerebral Cortex: ME, metabolism
Frontal Lobe: DE, drug effects
Frontal Lobe: ME, metabolism
*GTP-Binding Proteins: ME, metabolism
Guanine Nucleotides: PD, pharmacology
Guanylyl Imidodiphosphate: PD, pharmacology
Histocytochemistry
Paraffin Embedding
Parietal Lobe: DE, drug effects
Parietal Lobe: ME, metabolism
Receptors, Serotonin: DE, drug effects
*Receptors, Serotonin: ME, metabolism
Signal Transduction: DE, drug effects
Tetrahydronaphthalenes: ME, metabolism
RN **34273-04-6 (Guanylyl Imidodiphosphate)**; 78950-78-4 (8-Hydroxy-2-(di-n-propylamino)tetralin)
CN 0 (Guanine Nucleotides); 0 (Receptors, Serotonin); 0 (Tetrahydronaphthalenes); EC 3.6.1.- (GTP-Binding Proteins)

L143 ANSWER 10 OF 12 MEDLINE
AN **92099092** MEDLINE
DN **92099092** PubMed ID: **1684616**
TI Regional distribution of somatostatin receptor binding and modulation of adenylyl cyclase activity in Alzheimer's disease brain.
AU Bergstrom L; Garlind A; Nilsson L; Alafuzoff I; Fowler C J; Winblad B; Cowburn R F
CS Alzheimer's Disease Research Group, Karolinska Institute, Department of Geriatric Medicine, Huddinge, Sweden.
SO JOURNAL OF THE NEUROLOGICAL SCIENCES, **(1991 Oct)** 105 (2) 225-33.
Journal code: 0375403. ISSN: 0022-510X.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199202
ED Entered STN: 19920223
Last Updated on STN: 19980206
Entered Medline: 19920204
AB We have previously reported a reduction in the inhibitory effect of somatostatin on adenylyl cyclase activity in the superior temporal cortex of a group of Alzheimer's disease cases, compared to a group of matched controls. In the present study, the levels of high affinity 125I-Tyr11-somatostatin-14 binding, its modulation by guanine nucleotides and the effects of somatostatin on adenylyl cyclase activity have been measured in preparations of frontal cortex, hippocampus, caudate nucleus and cerebellum from the same patient and control groups. A significant reduction in 125I-Tyr11-somatostatin-14 binding was observed in the frontal cortex, but not other regions, of the Alzheimer's disease group, compared with control values. The profiles of inhibition of specific 125I-Tyr11-somatostatin-14 binding by Gpp(NH)p were similar in all regions in both groups. No significant differences in basal, forskolin-stimulated, or somatostatin and neuropeptide Y inhibitions of adenylyl cyclase activity were found between the two groups. The pattern of change of somatostatin binding in the Alzheimer's disease cases observed in the present study differs from the reported pattern of loss of somatostatin neurons and may be secondary to the degeneration of somatostatin receptor-bearing cholinergic afferents arising from the nucleus basalis.

The results of this study indicate that impaired somatostatin modulation of adenylyl cyclase is not a global phenomenon in Alzheimer's disease brain and also that there are no major disruptions of somatostatin receptor-G-protein coupling or of adenylyl cyclase catalytic activity in this disorder.

CT Check Tags: Human; Support, Non-U.S. Gov't
*Adenylate Cyclase: ME, metabolism
Aged
Aged, 80 and over
***Alzheimer Disease: ME, metabolism**
*Brain: ME, metabolism
Caudate Nucleus: ME, metabolism
Cerebellar Cortex: ME, metabolism
Cerebral Cortex: ME, metabolism
Guanylyl Imidodiphosphate: PD, pharmacology
Hippocampus: ME, metabolism
Kinetics
Organ Specificity
Receptors, Neurotransmitter: DE, drug effects
*Receptors, Neurotransmitter: ME, metabolism
Receptors, Somatostatin
Reference Values
*Somatostatin: ME, metabolism

RN **34273-04-6 (Guanylyl Imidodiphosphate)**; 51110-01-1 (Somatostatin)

CN 0 (Receptors, Neurotransmitter); 0 (Receptors, Somatostatin); EC 4.6.1.1 (Adenylate Cyclase)

L143 ANSWER 11 OF 12 MEDLINE

AN **91274844** MEDLINE

DN **91274844** PubMed ID: **2054615**

TI Reduced basal and stimulated (isoprenaline, Gpp(NH)p, forskolin) adenylate cyclase activity in Alzheimer's disease correlated with histopathological changes.

AU Ohm T G; Bohl J; Lemmer B

CS Zentrum der Morphologie, J.W. Goethe-Universitat, Frankfurt, Germany.

SO BRAIN RESEARCH, **(1991 Feb 1)** 540 (1-2) 229-36.
Journal code: 0045503. ISSN: 0006-8993.

CY Netherlands

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199107

ED Entered STN: 19910818
Last Updated on STN: 19980206
Entered Medline: 19910731

AB Cyclic adenosine monophosphate (cAMP) is an adenylate cyclase borne second messenger involved in basic metabolic events. The beta-adrenoceptor sensitive adenylate cyclase was studied in post-mortem hippocampi of controls and Alzheimer patients. Virtually identical subsets of each hippocampus homogenate were stimulated by 100 mumol isoprenaline, Gpp(NH)p and forskolin, respectively, in presence of an ATP-regenerating system. The determination of cAMP formed was carried out by means of a radioassay. The observed significant 50% reduction in basal as well as in stimulated adenylate cyclase activity in Alzheimer's disease is negatively correlated with semiquantitative evaluations of amyloid plaques (P less than 0.05) but not with neuritic plaques, neurofibrillary tangles or neuropil threads. This reduction in enzyme activity is obviously not due to simple cell loss alone. It is likely that the crucial point of the observed functional disturbance is at the level of the catalytic unit of the adenylate cyclase, since the same degree of reduction is maintained at all steps of the signal cascade.

CT Check Tags: Female; Human; Male; Support, Non-U.S. Gov't

*Adenylate Cyclase: ME, metabolism
Aged
Aged, 80 and over
***Alzheimer Disease: EN, enzymology**
Alzheimer Disease: PA, pathology
*Brain: EN, enzymology
Brain: PA, pathology
*Forskolin: PD, pharmacology
***Guanylyl Imidodiphosphate: PD, pharmacology**
*Isoproterenol: PD, pharmacology
Kinetics
Postmortem Changes
Reference Values
RN **34273-04-6 (Guanylyl Imidodiphosphate)**; 66428-89-5 (Forskolin); 7683-59-2 (Isoproterenol)
CN EC 4.6.1.1 (Adenylate Cyclase)

L143 ANSWER 12 OF 12 MEDLINE
AN **90099495** MEDLINE
DN **90099495** PubMed ID: **2557639**
TI Reduced cAMP-signal transduction in postmortem hippocampus of demented old people.
AU Ohm T G; Bohl J; Lemmer B
CS Zentren der Morphologie, J.W. Goethe-Universitat, Frankfurt, FRG.
SO PROGRESS IN CLINICAL AND BIOLOGICAL RESEARCH, **(1989)** 317 501-9.
Journal code: 7605701. ISSN: 0361-7742.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199001
ED Entered STN: 19900328
Last Updated on STN: 19980206
Entered Medline: 19900131
AB The basal as well as the stimulated activity of the adenylate cyclase was determined in postmortem hippocampi. The tissue probes were obtained from 12 demented individuals (10 Alzheimer-type dementia; 1 Down's syndrome; 1 argyrophilic grains syndrome) and from 15 age-matched controls. The diagnoses were done in accordance with histopathological criteria. Adenylate cyclase was stimulated by isoprenaline, Gpp(NH)p, or forskolin. The amount of cAMP formed was determined by the protein binding method using a radioimmuno assay. In tissues of controls as well as of demented patients adenylate cyclase was stimulated in the rank order of isoprenaline less than Gpp (NH) p less than forskolin. In hippocampal tissues of demented individuals a significant reduction (50%, p less than 0.01) in basal as well as stimulated adenylate cyclase activity was found. This reduction in cAMP signal transduction is not caused by simple cell loss.
CT Check Tags: Female; Human; Male
*Adenylate Cyclase: ME, metabolism
Aged
Alzheimer Disease: EN, enzymology
***Alzheimer Disease: ME, metabolism**
*Cyclic AMP: ME, metabolism
Enzyme Activation: DE, drug effects
Forskolin: PD, pharmacology
Guanylyl Imidodiphosphate: PD, pharmacology
Hippocampus: EN, enzymology
*Hippocampus: ME, metabolism
Isoproterenol: PD, pharmacology
Middle Age
*Signal Transduction
RN **34273-04-6 (Guanylyl Imidodiphosphate)**; 60-92-4 (Cyclic AMP);

66428-89-5 (Forskolin); 7683-59-2 (Isoproterenol)
CN EC 4.6.1.1 (Adenylate Cyclase)

=> fil biosis
FILE 'BIOSIS' ENTERED AT 09:47:31 ON 04 JUN 2003

FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 28 May 2003 (20030528/ED)

=> d all tot

L148 ANSWER 1 OF 2 BIOSIS
AN 2002:589372 BIOSIS
DN PREV200200589372
TI Inactivation of the human brain muscarinic acetylcholine receptor by oxidative damage catalyzed by a low molecular weight endogenous inhibitor from Alzheimer's brain is prevented by pyrophosphate analogs, bioflavonoids and other antioxidants.
AU **Fawcett, John R.**; Bordayo, Elizabeth Z.; Jackson, Kathy; Liu, Howard; Peterson, Jennifer; Svitak, Aleta; **Frey, William H., II (1)**
CS (1) Alzheimer's Research Center, HealthPartners Research Foundation, Regions Hospital, 640 Jackson Street, Saint Paul, MN, 55101-2595: alzheimr@tc.umn.edu USA
SO Brain Research, (20 September, 2002) Vol. 950, No. 1-2, pp. 10-20. http://www.elsevier.com/homepage/sah/bres/doc/journal2.htm. print. ISSN: 0006-8993.
DT Article
LA English
AB Oxidative stress has been implicated as a contributing factor to neurodegeneration in Alzheimer's disease. An endogenous, low molecular weight (LMW) inhibitor from Alzheimer's brain inactivates the human brain muscarinic acetylcholine receptor (mAChR). The inhibitor prevents agonist and antagonist binding to the mAChR as assesssed by radioligand binding studies. The LMW endogenous inhibitor, which has components with molecular weights between 100 and 1000 Da, requires dissolved oxygen and glutathione. Prevention of inactivation of the mAChR with peroxidase suggests that the LMW endogenous inhibitor generates peroxide. Heme, previously shown to be present in the LMW endogenous inhibitor, also inactivates the mAChR in the presence of peroxide. Free radical damage to the muscarinic receptor by the endogenous inhibitor can be prevented through the use of naturally occurring antioxidants including bilirubin, biliverdin, carnosol, myricetin and quericetin. In addition, pyrophosphate, imidodiphosphate, bisphosphonates and related compounds also protect the muscarinic receptor from free radical damage. Inactivation of the mAChR by the LMW endogenous inhibitor is likely to be a factor in the continual decline of Alzheimer's patients, even those taking acetylcholinesterase inhibitors. Natural antioxidants and pyrophosphate analogs may improve the effectiveness of acetylcholinesterase inhibitors and prove useful in the treatment and prevention of Alzheimer's disease since the muscarinic acetylcholine receptor is required for memory, and decreased cholinergic function is a critical deficit in Alzheimer's disease.
CC Biochemical Studies - General *10060
Behavioral Biology - Human Behavior *07004
Biochemical Studies - Proteins, Peptides and Amino Acids *10064
Biochemical Studies - Porphyrins and Bile Pigments *10065

Enzymes - General and Comparative Studies; Coenzymes *10802
Nervous System - Physiology and Biochemistry *20504
Nervous System - Pathology *20506
Psychiatry - Psychopathology; Psychodynamics and Therapy *21002
BC Hominidae 86215
IT Major Concepts
Biochemistry and Molecular Biophysics; Nervous System (Neural Coordination)
IT Parts, Structures, & Systems of Organisms
brain: nervous system
IT Diseases
Alzheimer's disease: behavioral and mental disorders, nervous system disease
IT Chemicals & Biochemicals
acetylcholinesterase inhibitors; antioxidants; bilirubin; biliverdin; bioflavonoids; bisphosphonates; carnosol; glutathione; imidodiphosphate; muscarinic acetylcholine receptor: inactivation; muscarinic receptor; myricetin; oxygen; peroxidase; phosphate analogs; pyrophosphate; quericetin
IT Alternate Indexing
Alzheimer Disease (MeSH)
IT Methods & Equipment
radioligand binding studies: assessment method, radiobiology method
ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
human (Hominidae)
ORGN Organism Superterms
Animals; Chordates; Humans; Mammals; Primates; Vertebrates
RN 635-65-4 (BILIRUBIN)
114-25-0 (BILIVERDIN)
5957-80-2 (CARNOSOL)
70-18-8 (GLUTATHIONE)
112319-85-4 (IMIDODIPHOSPHATE)
529-44-2 (MYRICETIN)
7782-44-7 (OXYGEN)
9003-99-0 (PEROXIDASE)
14000-31-8 (PYROPHOSPHATE)

L148 ANSWER 2 OF 2 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 2002:368901 BIOSIS
DN PREV200200368901
TI Protection of the human brain muscarinic acetylcholine receptor from damage by free radicals generated by an endogenous, low molecular weight inhibitor isolated from Alzheimer's disease brain.
AU Bordayo, Elizabeth Z. (1); **Fawcett, John R. (1); Frey, William H., II (1)**
CS (1) Alzheimer's Research, HealthPartners Research Foundation, 640 Jackson Street, Saint Paul, MN, 55101 USA
SO FASEB Journal, (March 20, 2002) Vol. 16, No. 4, pp. A546. http://www.fasebj.org/. print.
Meeting Info.: Annual Meeting of the Professional Research Scientists on Experimental Biology New Orleans, Louisiana, USA April 20-24, 2002
ISSN: 0892-6638.
DT Conference
LA English
AB Current Alzheimer's disease (AD) treatment focuses on the use of cholinesterase inhibitors to increase acetylcholine. This mechanism will only be beneficial if there are viable muscarinic acetylcholine receptors (mAChR) to bind the acetylcholine. In AD brain there is an elevation of a low molecular weight (LMW) inhibitor containing heme that can oxidatively damage the mAChR. This may decrease the efficacy of anticholinesterase therapy. Agonist and antagonist binding to the human brain mAChR was

assessed using radioligand-binding assays. The mAChR was exposed to the LMW inhibitor in the presence and absence of various compounds to determine their effectiveness at protecting the mAChR from oxidative damage. Bile pigments (bilirubin and biliverdin), flavonoids (myricetin and quercetin) and diphosphates (pyrophosphate, imidodiphosphate and bisphosphonate) are hundreds of times more effective than vitamin E at protecting the mAChR. Protecting the human brain mAChR from oxidative stress in aging and AD should help to maintain memory function and increase the effectiveness of cholinesterase inhibitors, cholinergic agonists and related therapeutic agents.

CC General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals *00520
Behavioral Biology - Human Behavior *07004
Biochemical Studies - General *10060
Nervous System - Physiology and Biochemistry *20504
Nervous System - Pathology *20506
Psychiatry - Psychopathology; Psychodynamics and Therapy *21002

BC Hominidae 86215

IT Major Concepts
Nervous System (Neural Coordination)

IT Diseases
Alzheimer's disease: behavioral and mental disorders, nervous system disease

IT Chemicals & Biochemicals
bile pigments: free radical-induced muscarinic acetylcholine receptor damage protective effects; diphosphates: free radical-induced muscarinic acetylcholine receptor damage protective effects; endogenous low molecular weight inhibitor protein: Alzheimer disease brain isolation, free radical generation, muscarinic acetylcholine receptor damage inducer; flavonoids: free radical-induced muscarinic acetylcholine receptor damage protective effects

IT Alternate Indexing
Alzheimer Disease (MeSH)

IT Miscellaneous Descriptors
Meeting Abstract

ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name
human (Hominidae): normal subjects

ORGN Organism Superterms
Animals; Chordates; Humans; Mammals; Primates; Vertebrates

RN **14000-31-8** (DIPHOSPHATES)

=> fil wpix
FILE 'WPIX' ENTERED AT 10:18:01 ON 04 JUN 2003

FILE LAST UPDATED: 3 JUN 2003 <20030603/UP>
MOST RECENT DERWENT UPDATE: 200335 <200335/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

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=> d all abeq tech abex tot

L178 ANSWER 1 OF 3 WPIX (C) 2003 THOMSON DERWENT
AN **2002-082826** [11] WPIX
DNC **C2002-025015**
TI New method for protecting a tissue component in a subject comprises administering at least one **pyrophosphate** analog, the subject suffers such things as cancer or **Alzheimer**'s disease.
DC B05
IN CHEN, X; **FAWCETT, J R; FREY, W H;** THORNE, R G
PA (FAWC-I) FAWCETT J R; (FREY-I) FREY W H; (HEAL-N) **HEALTHPARTNERS RES FOUND**
CYC 95
PI WO 2001082932 A2 20011108 (200211)* EN 77p A61K031-661 <--
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
US 2002028786 A1 20020307 (200221) A61K031-7105 <--
AU 2001057444 A 20011112 (200223) A61K031-661 <--
EP 1278525 A2 20030129 (200310) EN A61K031-661 <--
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR
ADT WO 2001082932 A2 WO 2001-US13931 20010430; US 2002028786 A1 Provisional US 2000-200843P 20000501, Provisional US 2000-230263P 20000906, Provisional US 2000-233025P 20000915, US 2001-844450 20010427; AU 2001057444 A AU 2001-57444 20010430; EP 1278525 A2 EP 2001-930957 20010430, WO 2001-US13931 20010430
FDT AU 2001057444 A Based on WO 200182932; EP 1278525 A2 Based on WO 200182932
PRAI US 2000-233025P 20000915; US 2000-200843P 20000501; US 2000-230263P 20000906; US 2001-844450 20010427
IC ICM **A61K031-661; A61K031-7105**
ICS **A61K031-66; A61K031-6615; A61K031-662; A61K031-706; A61K031-7076; A61K031-7084**
AB WO 200182932 A UPAB: 20020215
NOVELTY - A method of protecting a tissue component in a subject comprises administering at least one **pyrophosphate** analog.
DETAILED DESCRIPTION - A method of protecting a tissue component in a subject comprises administering at least one **pyrophosphate** analog of formula (I) or (II) or a dinucleoside-5-5'-**pyrophosphate**, a **cyclopyrophosphate** of purine, a pyrimidine acyclonucleoside, an inositol diphosphate, an inositol triphosphate, an inositol tetraphosphate, an inositol pentaphosphate, an inositol hexaphosphate or their salt.
X = O, CH2, NH or S;
R1 = H, lower alkyl, guanyl, adenylyl, glycerol, acyl glycerol, diacyl glycerol, serine, threonine, tyrosine, arachidonyl, -PO(OH)(OR2), or -(PO(OH)O)m-PO(OH)(OR2);
m = 1-3;
R2 = H, lower alkyl, guanyl, adenylyl, glycerol, acyl glycerol, diacyl glycerol, serine, threonine, tyrosine, or arachidonyl; and
n = 1-900.
p = 2-4;

Y = O, RCR3, CR, C (p=4), CH (p=3), or CH2 (p=2), NH, N, S;
R, R3 = H, OH, lower alkyl, or (CH2)qNH2; and
q = 1-6.

INDEPENDENT CLAIMS are included for:
(1) a method of protecting tissue from oxidative stress;
(2) a method of increasing the efficacy of an agent that affects a receptor;
(3) a method of protecting a subject from at least one carcinogenic metal;
(4) a method of reducing poisoning of a subject by at least one metal;
(5) a method (e) of treating bacterial, fungal, algo, or algae infections;
(6) a method of reducing toxic actions of metal ions;
(7) a method (g) of protecting a pharmacological agent in a formulation; and
(8) a method (h) of increasing efficacy of a neurologic agent.

ACTIVITY - Cytostatic; cardiant; hypotensive; vasotropic; antiinflammatory; uropathic; antidiabetic; immunosuppressive; osteopathic; nootropic; neuroprotective; cerebroprotective; tranquilizer; neuroleptic; antitumor.

MECHANISM OF ACTION - Muscarinic acetylcholine receptor modulator.

USE - The methods are used on subjects suffering from cancer, neuropathies, diseases or disorders of the heart, smooth muscles, blood, blood vessels, glands, or bones, hypertension, myocardial infarction, ischemic heart disease or congestive heart failure, irritable bowel syndrome, diverticular disease, urinary incontinence, esophageal achalasia, chronic obstructive airways disease, cardiac arrhythmia, xerostomia, diabetes mellitus, Sjogren's syndrome, Paget's disease, hereditary hematochromatosis, a non-CNS disorder resulting from normal aging, a neurologic disorder, a psychiatric disorder, **Alzheimer**'s disease, Parkinson's disease, Lewy body dementia, multiple sclerosis, cerebellar ataxia, progressive supranuclear palsy, amyotrophic lateral sclerosis, an affective disorder, an anxiety disorder, schizophrenia, cell damage, nerve damage, a CNS infection, a tumor of the brain, a tumor of the spinal cord, a stroke in the brain, a stroke in the spinal cord, a prion disease, a CNS disorder resulting from ordinary aging, a brain injury, a spinal cord injury, or a non-CNS disorder resulting from normal aging.

Dwg.0/20

FS CPI

FA AB; GI; DCN

MC CPI: **B05-B01G**; **B05-B01J**; **B05-B01P**; B06-D09; B07-A02A; B10-A17; B10-B02E; B10-B02H; B10-E04C; B14-E10C; B14-F01; B14-F01B; B14-F01E; B14-F02; B14-F02B; B14-G02; B14-H01; B14-H01B; B14-J01; B14-J01A3; **B14-J01A4**; B14-J01B3; B14-J01B4; B14-J05; B14-L01; B14-L06; B14-N01; B14-N16; B14-S01; B14-S04

TECH UPTX: 20020215

TECHNOLOGY FOCUS - BIOLOGY - Preferred tissue: The tissue component is at least one of receptor, a protein, a lipid, a nucleic acid, a carbohydrate, a hormone, a vitamin and a cofactor.

Preferred receptor: The receptor is for a neurotransmitter, a neuropeptide, a neurotrophin, a growth factor, a steroid, a histamine, a purine, a benzodiazepine, arachidonic acid, nitric oxide, carbon monoxide, an odorant, or an ion channel. When the method is for increasing the efficacy of an agent that affects a receptor, the receptor is one of muscarinic acetylcholine, nicotinic acetylcholine, an opiate, a catecholamine, serotonin, glutamate, aspartate, cannabinoid, gamma aminobutyric acid, or glycine.

Preferred agent: The agent affects a muscarinic acetylcholine receptor and comprises an anticholinesterase agent, a neurologic agent, a muscarinic receptor agonist, xanomeline, donepezil, rivastigmine, galanthamine, metrifonate. The pharmacological agent in method (g) is a therapeutic or

diagnostic agent. The neurologic agent comprises a ganglioside (comprising GM-1 ganglioside), a phosphatidylserine, a nerve growth factor, a neurotrophin (comprising neurotrophin 3, 4 and/or 5), a brain-derived neurotrophic factor, a fibroblast growth factor (comprising basic fibroblast growth factor or acidic fibroblast growth factor), an insulin, an insulin-like growth factor (comprising insulin-like growth factor-I and/or 2), a transforming growth factor, an epidermal growth factor, a platelet-derived growth factor, a neurokine, activity-dependent neurotrophic factor, a ciliary neurotrophic factor, a glia-derived neurotrophic factor, a glia-derived nexin, a cholinergic enhancing factor (which comprises ethanolamine, thyroid hormone T. 3 and/or gallamine), an antisense oligonucleotide, a DNA or RNA vector or plasmid that encodes one or more protein neurologic agents and/or nerve growth promoting factors. Preferred method: The subject in method (e) is a plant, an animal or a mammal.

TECHNOLOGY FOCUS - INORGANIC CHEMISTRY - Preferred metal: The carcinogenic metal is arsenic, cadmium, cobalt, nickel, lead or chromium. The metal is iron, copper, mercury, lead, cadmium, vanadium or their alloys. The metal ions are Fe++, Hg++, Cd++, Cu++, As++ or Pb++.

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred method: The methods further comprise combining any **pyrophosphate** analog with bilirubin, biliverdin, carnosol, quercetin, myricetin, bioflavinoid, heme oxygenase, a vector encoding a heme oxygenase, heme oxygenase-1, a vector encoding a heme oxygenase-1, heme oxygenase-2, a vector encoding a biliverdin reductase, a catalase, a vector encoding a catalase, a peroxidase, a vector encoding a peroxidase, and/or a heme binding protein (which comprises hemopexin and/or a lipoprotein).

ABEX UPTX: 20020215

SPECIFIC COMPOUNDS - The **pyrophosphate** in method (e) comprises imidodiphosphate. Preferably the **pyrophosphate** analog comprises imidodiphosphate, guanylimidodiphosphate, adenylylimidodiphosphate, etidronic acid, and/or pamidronic acid.

L178 ANSWER 2 OF 3 WPIX (C) 2003 THOMSON DERWENT
AN 2000-431196 [37] WPIX
DNC C2000-130995
TI Administration of agent to the central nervous system (CNS) via tissue innervated by the trigeminal nerve, used in the treatment and diagnosis of diseases and disorders of the CNS, brain and spinal cord..
DC A14 A17 A96 B07
IN CHEN, X; **FREY, W H**; THORNE, R G
PA (CHIR) CHIRON CORP
CYC 90
PI WO 2000033814 A2 20000615 (200037)* EN 54p A61K009-00
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
AU 2000021734 A 20000626 (200045) A61K009-00
EP 1135105 A2 20010926 (200157) EN A61K009-00
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
JP 2002531490 W 20020924 (200278) 72p A61K009-08
ADT WO 2000033814 A2 WO 1999-US29335 19991209; AU 2000021734 A AU 2000-21734 19991209; EP 1135105 A2 EP 1999-966114 19991209, WO 1999-US29335 19991209; JP 2002531490 W WO 1999-US29335 19991209, JP 2000-586308 19991209
FDT AU 2000021734 A Based on WO 200033814; EP 1135105 A2 Based on WO 200033814; JP 2002531490 W Based on WO 200033814
PRAI US 1998-208539 19981209

IC ICM A61K009-00; A61K009-08
ICS A61K009-06; A61K009-107; A61K009-12; A61K009-127; A61K038-00; A61K038-28; A61K045-00; A61K047-24; A61K047-32; A61P025-00; A61P025-08; A61P025-18; A61P025-22; A61P025-24; A61P025-28; A61P027-16; A61P031-18; A61P031-22; A61P035-00

AB WO 200033814 A UPAB: 20000807
NOVELTY - A method of delivering agents to the central nervous system (CNS) comprises administering a composition comprising the agent to a tissue innervated by the trigeminal nerve and outside the nasal cavity, wherein the agent is absorbed through the tissue and is transported to the CNS.

USE - The method can be used to deliver agents to the CNS including the spine and the brain for diagnosis, treatment or prevention of disorders or diseases of the CNS, brain or spinal cord. The disorders may be neurologic or psychiatric and include **Alzheimer**'s disease, Parkinson's disease, Lewy body dementia, multiple sclerosis, epilepsy, cerebellar ataxia, progressive supranuclear palsy, amyotrophic lateral sclerosis, affective disorders, anxiety disorders, obsessive compulsive disorders, personality disorders, attention deficit disorders, attention deficit hyperacativity disorder, Tourette syndrome, Tay Sachs, Nieman Pick and other lipid storage and genetic brain diseases and schizophrenia. The method can also be used in patients suffering from or at risk of nerve damage from cerebrovascular disorders such as stroke, from CNS infections including meningitis and human immunodeficiency virus (HIV), from tumors of the brain and spinal cord or from prion disease, to counter CNS disorders resulting from aging, from brain injury or from spinal cord injury or to treat neurodegenerative disorders.

ADVANTAGE - The method is non-invasive, unlike most methods for administration to the CNS.

Dwg.0/0

FS CPI

FA AB; DCN

MC CPI: A04-G07; A12-V01; A12-V03C2; B04-B01B; B04-B03C; B04-C01; B04-C03; B04-D01; B04-E01; B04-E08; B04-H06; B04-H06G; **B05-B01P**; B12-M05; B14-A02B1; B14-H01; B14-J01; B14-J07; B14-N16; B14-S01

TECH UPTX: 20000807
TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Tissue: The agent is administered to tissue innervated by the trigeminal nerve but outside the nasal cavity, therefore it may be administered to oral tissue e.g. teeth, the gums, the floor of the oral cavity, the cheeks, the lips, the tongue or a combination thereof; to mucosa or epithelium innervated by the trigeminal nerve e.g. mucosa or epithelium of or surrounding the eye, such as mucosa or epithelium of the upper eyelid, the lower eyelid, the eyeballs, the conjunctiva, the lacrimal system or a combination thereof; to the skin of the face, scalp or temporal region suitable skin of the face includes skin of the chin, the upper lip, the forehead, the nose, the cheek, skin around the eyes and combinations thereof; or to tissue of or around the ear e.g. the auricle, the external acoustic meatus, the tympanic membrane, skin in the temporal region especially skin of the temple and the lateral part of the scalp and combinations thereof. Preferred Agents: Agents that can be delivered to the CNS include organic pharmaceuticals, inorganic molecules, peptides, peptoids, proteins, lipids, carbohydrates, nucelic acids or diagnostic agents. Preferred neurologic agents include GM1 ganglioside, fibroblast growth factor especially basic fibroblast growth factor, insulin-like growth factor especially insulin-like growth factor 1, phosphatidyl serine, a plasmid, a vector, an antisense oligonucleotide etc. Preferred Compositions: The composition may comprise a liquid, powder, spray, gel, ointment, infusion or a combination thereof. The composition comprises the active agent and a carrier, additive and/or adjuvant. Among the optional substances in the composition lipophilic substances that can enhance absorption of the agent are particularly preferred. The agent may be mixed with a lipophilic adjuvant alone or in combination with a carrier or may be combined with

one of several types of micelle or liposome substances. Lipophilic micelles and liposomes preferably comprise a ganglioside, a phosphatidylcholine, a phosphatidylserine, lipofectin, DOTAP or a combination thereof. The composition may additionally contain a controlled release polymer comprising a poly(ethylene-co-vinylacetate) especially for sub-lingual administration.
Preferred Route: The agent is transported along a neural pathway which comprises lymphatic channels running with a nerve and is transported to the CNS including to a hippocampal formation, an amygdaloid nuclei, a nucleus basalis of Meynert, a locus ceruleus, a brainstem raphe nuclei or combinations thereof, the spinal cord, the brain stem, a cortical structure, a subcortical structure and any combinations thereof.

ABEX UPTX: 20000807

ADMINISTRATION - Administration may be continuous or intermittent. Dosage is dependent on a wide variety of factors.

EXAMPLE - Male Sprague-Dawley rats, 200-310g, were anesthetized with intraperitoneal pentobarbital (40 mg/kg). Drug delivery to the brain and spinal cord was assessed after sublingual administration of 7.4 nmol of 125I-IGF-I (insulin-like growth factor I) in phosphate buffered saline, pH 7.4. Rats were placed in on their bellies with posterior elevated and mouth lowered. 125I-IGF-I on a small strip of filter paper was placed under the tongue. The rats subsequently underwent perfusion-fixation within minutes following completion of administration. Areas dissected included selected brain regions and the cervical, thoracic and sacral regions of the spinal cord. Rapid appearance of neurologic agent in the brain and spinal cord was observed by determining the radioactivity. The concentration of the neurologic agent was higher in the cervical region of the spinal cord than in the thoracic region, and was higher in the thoracic region than in the sacral or lumbar regions. High concentrations were found in the meninges or dura surrounding each of the following: the olfactory bulb, the dorsal and ventral regions of the brain, the trigeminal nerve and the upper cervical spinal cord. The IGF was also found in the olfactory bulb, spinal cord and the brain stem.The trigeminal nerve itself contained high concentrations of the neurologic agent.

L178 ANSWER 3 OF 3 WPIX (C) 2003 THOMSON DERWENT
AN 2000-431195 [37] WPIX
DNC C2000-130994
TI Administration of a neurotrophic agent to the central nervous system (CNS) via administration to the nasal cavity used in the treatment and diagnosis of disorders and diseases of the CNS, brain and spinal cord..
DC A14 A17 A96 B07
IN CHEN, X; **FREY, W H**; THORNE, R G
PA (CHIR) CHIRON CORP
CYC 90
PI WO 2000033813 A1 20000615 (200037)* EN 62p A61K009-00
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
AU 2000020495 A 20000626 (200045) A61K009-00
EP 1137401 A1 20011004 (200158) EN A61K009-00
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MK RO SI
JP 2002531489 W 20020924 (200278) 74p A61K045-00
ADT WO 2000033813 A1 WO 1999-US29334 19991209; AU 2000020495 A AU 2000-20495 19991209; EP 1137401 A1 EP 1999-964208 19991209, WO 1999-US29334 19991209; JP 2002531489 W WO 1999-US29334 19991209, JP 2000-586307 19991209
FDT AU 2000020495 A Based on WO 200033813; EP 1137401 A1 Based on WO 200033813; JP 2002531489 W Based on WO 200033813
PRAI US 1998-208538 19981209

IC ICM A61K009-00; A61K045-00
ICS A61K009-06; A61K009-08; A61K009-12; A61K009-127; A61K009-14; A61K009-72; A61K038-00; A61K047-24; A61K047-30; A61K047-32; A61K047-36; A61P003-02; A61P025-00; A61P025-08; A61P025-16; A61P025-18; A61P025-22; A61P025-28

AB WO 200033813 A UPAB: 20000807
NOVELTY - Method for transporting a neurotrophic agent to the central nervous system (CNS) comprises administering the agent to the upper third of the nasal cavity, wherein the neurotrophic agent is absorbed through the nasal cavity and transported to the CNS.

USE - The method can be used to deliver agents to the CNS including the spine and the brain for diagnosis, treatment or prevention of disorders or diseases of the CNS, brain or spinal cord. The disorders may be neurologic or psychiatric and include **Alzheimer**'s disease, Parkinson's disease, Lewy body dementia, multiple sclerosis, epilepsy, cerebellar ataxia, progressive supranuclear palsy, amyotrophic lateral sclerosis, affective disorders, anxiety disorders, obsessive compulsive disorders, personality disorders, attention deficit disorders, attention deficit hyperactivity disorder, Tourette syndrome, Tay Sachs, Nieman Pick and other lipid storage and genetic brain diseases and schizophrenia. The method can also be used in patients suffering from or at risk of nerve damage from cerebrovascular disorders such as stroke, from CNS infections including meningitis and HIV, from tumors of the brain and spinal cord or from prion disease, to counter CNS disorders resulting from aging, from brain injury or from spinal cord injury or to treat neurodegenerative disorders.

ADVANTAGE - The method is non-invasive, unlike most methods for administration to the CNS.

Dwg.0/5

FS CPI
FA AB; DCN
MC CPI: A04-G07; A12-V01; A12-V03C2; B04-B01B; B04-C03B; B04-H06; B04-H06D; B04-H06G; **B05-B01P**; B12-M01B; B14-A02B1; B14-J01; B14-N16
TECH UPTX: 20000807

TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Administration: The agent is administered to tissue innervated by the trigeminal and olfactory nerves inside the nasal cavity and sinuses. The agent is delivered to the olfactory area in the upper third of the nasal cavity and particularly to the olfactory epithelium in the roof of the nose.
Preferred Agents: Neurotrophic agents that can be delivered to the CNS include fibroblast growth factor especially basic fibroblast growth factor, insulin-like growth factor especially insulin-like growth factor 1 and nerve growth factor.
Preferred Compositions: The composition may comprise a liquid, powder, spray, gel, ointment, infusion or a combination thereof. The composition comprises the active agent and a carrier, additive and/or adjuvant. Among the optional substances in the composition lipophilic substances that can enhance absorption of the agent are particularly preferred. The agent may be mixed with a lipophilic adjuvant alone or in combination with a carrier or may be combined with one of several types of micelle or liposome substances. Lipophilic micelles and liposomes preferably comprise a ganglioside, a phosphatidylcholine, a phosphatidylserine, lipofectin, DOTAP or a combination thereof. The composition may additionally contain a controlled release polymer comprising a poly(ethylene-co-vinylacetate).
Preferred Route: The agent is transported along a neural pathway, either trigeminal or olfactory nerve pathway, which comprises lymphatic channels running with a nerve and is transported to the CNS including to an olfactory bulb, a hippocampal formation, a frontal cortex, a midbrain, a brainstem, a spinal cord or a combination thereof.

TECHNOLOGY FOCUS - POLYMERS - Preferred Composition: The composition for administration to the CNS may comprise neurologic agents including fibroblast growth factor especially basic fibroblast growth factor,

insulin-like growth factor especially insulin-like growth factor 1 and nerve growth factor. The composition may comprise a controlled release polymer comprising a poly(ethylene-co-vinylacetate). The composition preferably also comprises a lipophilic adjuvant alone or in combination with a carrier or may be combined with one of several types of micelle or liposome substance.

ABEX UPTX: 20000807

ADMINISTRATION - Administration may be continuous or intermittent. Dosage is approximately 0.1-10 nmol of the neurotrophic agent, resulting in a therapeutically effective amount of 10-11M to about 10-9 M in a portion of the CNS.

EXAMPLE - Male Sprague-Dawley rats, 200-310 g, were anesthetized with intraperitoneal pentobarbital (40 mg/kg). Drug delivery to the brain and spinal cord was assessed after intranasal administration of 7.4 nmol of 125I-IGF-I (insulin-like growth factor I) in phosphate buffered saline, pH 7.4. Rats were placed on their backs and administered about 25 microlitres of 125I-IGF-I to each naris over 10-22 minutes, alternating drops every 2-3 minutes between the left and right nares. The rats subsequently underwent perfusion-fixation within minutes following completion of administration. Areas dissected included the olfactory bulbs, medulla, pons and cerebellum. Rapid appearance of radiolabel in the brain observed with the highest concentrations seen in the olfactory bulbs (3 + 0.47 nM), medulla (0.62 +0.16 nm), pons (0.31 +0.07 nm) and cerebellum (0.3 +0.1 nm).

=> d his

(FILE 'HOME' ENTERED AT 08:06:33 ON 04 JUN 2003)
SET COST OFF

FILE 'HCAPLUS' ENTERED AT 08:06:47 ON 04 JUN 2003
E US20020028786/PN
L1 1 S E3
E WO2001-US13931/AP,PRN
L2 1 S E3,E4
E US2000-233263/AP,PRN
L3 1 S E5
E US2000-233025/AP,PRN
L4 1 S E5
E US2000-230263/AP,PRN
L5 1 S E5
L6 1 S L1-L5
E HEALTHPARTNER/PA,CS
L7 12 S E5-E11
E HEALTH PARTNER/PA,CS
L8 23 S (HEALTH(L)PARTN?)/PA,CS
SEL DN AN 23
L9 1 S L8 AND E1-E3
L10 13 S L7,L9
E FREY W/AU
L11 167 S E3,E7-E9,E25,E29-E33
E FAWCETT J/AU
L12 33 S E3,E13
E FAWCETT JOHN/AU
L13 171 S E3,E6,E7
L14 48821 S ?PYROPHOS?
L15 144 S ?PYRO PHOS?
E PYROPHOS/CT
E E16+ALL
L16 851 S E1
E E2+ALL

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L17        8258 S E10+NT
                E E8+ALL
L18       24848 S E4+NT
                E E3+ALL
L19      219974 S E3+NT
L20           2 S L10 AND L14-L19
L21           3 S L11-L13 AND L14-L19
L22           3 S L6,L20,L21
L23           2 S L22 NOT RHODIUM/TI
                E ALZHEIMER/CT
L24       11589 S E3-E20
                E E9+ALL
L25       11603 S E6,E5+NT
L26       11213 S E23+NT OR E24+NT OR E25+NT OR E26+NT OR E27+NT OR E28+NT OR E
                E E23+ALL
L27        1188 S E8
                E E6+ALL
L28       72281 S E7,E6+NT
                E E22+ALL
                E E5+ALL
                E E25+ALL
L29       10751 S E9+NT
                E E8+ALL
L30        2080 S E6,E5+NT
L31       28838 S E15+NT OR E13+NT
                E E10+ALL
                E E27+ALL
L32         449 S E8-E11
                E E14+ALL
                E E28+ALL
                E E3+ALL
                E E29+ALL
L33         961 S E3
L34           3 S L10 AND L24-L33
L35          14 S L11-L13 AND L24-L33
L36          14 S L23,L34,L35
L37           4 S L36 AND ?PHOSPH?
L38           2 S L37 AND L23
                SEL RN

    FILE 'REGISTRY' ENTERED AT 08:21:28 ON 04 JUN 2003
L39          66 S E1-E67
L40          14 S L39 AND P/ELS
L41           3 S L40 AND (C4H8CL3O4P OR C2H8O7P2 OR C3H11NO7P2)
L42           1 S L40 AND H3O3P
L43           2 S L41 AND P>=2
L44          10 S L40 NOT L41,L42
L45          12 S L43,L44
L46         151 S (C6H16O18P4 OR C6H15O15P3 OR C6H14O12P2)/MF AND 46.150.1/RID
L47           9 S 2466-09-3 OR 10380-08-2 OR 13813-62-2 OR 12395-97-0 OR 29444-
L48           1 S 7664-38-2
L49          10 S L47,L48
                SEL RN
L50       16644 S E68-E77/CRN
L51        2775 S L50 AND PMS/CI
L52         232 S L51 AND HOMOPOLYMER
L53         117 S L52 AND NR>=1
L54         115 S L52 NOT L53
L55          16 S L54 AND (LI OR H3N OR NA)
L56           4 S L55 AND 2/NC
L57           8 S L55 AND 3/NC
L58           1 S L57 AND K
L59           5 S L56,L58
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L60        2543 S L51 NOT L52-L59
L61        1751 S L60 AND NR>=1
L62         792 S L60 NOT L61
L63         363 S L62 NOT (C2H4O OR C3H6O)
L64         142 S L63 NOT (N OR S OR SI)/ELS
L65        2697 S L51 AND H3O4P
L66           5 S L65 AND 1/NC
L67           2 S L40 NOT L45
L68           1 S L67 AND H3O3P
L69          22 S L45,L49,L68
L70         170 S L46,L69
L71          10 S (O7P2 OR O13P4 OR O16P5 OR O19P6 OR O22P7 OR O25P8 OR L28P9 O
L72         180 S L70,L71
                E HEXAMETAPHOSPHATE/CN
L73           1 S E3
L74           2 S E4,E5
                E OPOP/ES
L75        1511 S (OPOP OR OPOPOP OR OPOPOP OR OPOPOPOP OR OPOPOPOPOP OR OPOPOP
L76         177 S L75 AND 1/NR AND 1/NC
L77         162 S L76 NOT (ETHOXY OR METHOXY OR PROPOXY)
L78         134 S L77 NOT (TIS OR AYS OR MNS)/CI
L79         132 S L78 NOT CCS/CI
L80          50 S L79 NOT (C OR F OR CL OR S OR N)/ELS
L81          41 S L80 NOT RPS/CI
L82          35 S L81 NOT ION
L83           9 S L82 AND (H2O6P2 OR H3O8P3 OR H4O12P4 OR H5O15P5 OR H6O18P6 OR
L84           6 S L83 NOT 3-4/P
L85           3 S L83 NOT L84
L86           1 S L85 NOT OPOPOP/ES
L87           7 S L84,L86
L88           2 S L75 AND H9O27P9
L89         268 S L75 AND H3O9P3
L90           1 S L89 AND 1/NC
L91           8 S L87,L90
L92         188 S L72,L91
                E GLASS/CN
L93           1 S E56
L94         189 S L92,L93

     FILE 'HCAPLUS' ENTERED AT 09:07:16 ON 04 JUN 2003
L95       81393 S L94
L96        5383 S INOSITOL(L)(DIPHOSPH? OR TRIPHOS? OR TETRAPHOS? OR PENTAPHOS?
L97       82822 S IMIDODIPHOS? OR GUANYLIMIDODIPHOS? OR ADENYLYLIMIDODIPHOS? OR
L98         111 S (ETIDRONIC OR PAMIDRONIC)()ACID

     FILE 'REGISTRY' ENTERED AT 09:08:54 ON 04 JUN 2003

     FILE 'HCAPLUS' ENTERED AT 09:11:24 ON 04 JUN 2003
L99         991 S AMIDRONIC ACID OR (GUANYL? OR ADENYL?)()IMIDODIPHOSPH?
L100     156796 S L95-L98,L99
L101       1483 S L24-L33 AND L100
L102         17 S L10-L13 AND L100
L103          2 S L101 AND L102
L104          2 S L38,L103
L105         15 S L102 NOT L104
L106         91 S L100 (L) THU/RL AND L101
L107         66 S L95 (L) THU/RL AND L106
L108         12 S L107 AND ?ALZHEIM?
L109          9 S L107 AND ?AMYLO?
L110         19 S L108,L109
L111       1277 S L101 AND (PD<=20000501 OR PRD<=20000501 OR AD<=20000501)
L112         63 S L111 AND L106
L113         10 S L110 AND L112
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                SEL DN AN 2 3 4 5 6
L114          5 S E1-E15 AND L113
L115         53 S L112 NOT L113
                SEL DN AN 16 28 27 42
L116          4 S E16-E27 AND L115
L117         10 S L114,L116,L104
                SEL HIT RN

     FILE 'REGISTRY' ENTERED AT 09:25:37 ON 04 JUN 2003
L118         16 S E28-E43
L119         15 S L118 NOT UNSPECIFIED

     FILE 'REGISTRY' ENTERED AT 09:26:07 ON 04 JUN 2003

     FILE 'HCAPLUS' ENTERED AT 09:26:19 ON 04 JUN 2003

     FILE 'MEDLINE' ENTERED AT 09:26:56 ON 04 JUN 2003
L120      12812 S L94
L121      72485 S L97,L98,L99
                E PYROPHOSPHATE/CT
                E E20+ALL
                E E2+ALL
L122       4763 S E17,E21
L123       4763 S E17,E21/CN
                E E16+ALL
L124        638 S E16
L125        638 S E16/CN
L126      79693 S L120-L125
                E ALZHEIMER/CT
                E E8+ALL
L127      37424 S E12+NT OR E46+NT OR E47+NT OR E48+NT OR E49+NT OR E50+NT OR E
L128        119 S L126 AND L127
L129        105 S L128 AND PY<=2000
L130          4 S L129 NOT AB/FA
L131        101 S L129 NOT L130
L132          3 S L131 AND OXIDATIVE STRESS
L133         98 S L131 NOT L132
                SEL DN AN 29 30 58 65 67 78 80 81 85 86 90
L134         11 S E1-E33
L135         11 S L134 AND L120-L134
                E FREYW/AU
                E FREY W/AU
L136        109 S E3,E4,E12,E13,E21,E22
                E FAWCETT J/AU
L137        284 S E3,E13
                E E24
L138          1 S E5
L139          5 S L126 AND L136-L138
L140          1 S L139 AND ?ALZHEIM?
L141          1 S L139 AND L128
L142          1 S L140,L141
L143         12 S L135,L142

     FILE 'MEDLINE' ENTERED AT 09:45:59 ON 04 JUN 2003

     FILE 'BIOSIS' ENTERED AT 09:46:08 ON 04 JUN 2003
                E FREY W/AU
L144        178 S E3,E7-E12,E20-E24
                E FAWCETT J/AU
L145        119 S E3,E12
L146         11 S E28,E30
L147        295 S L144-L146
L148          2 S L147 AND L94
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FILE 'BIOSIS' ENTERED AT 09:47:31 ON 04 JUN 2003

FILE 'WPIX' ENTERED AT 09:47:56 ON 04 JUN 2003

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                E FREY W/AU
L149         120 S E3,E7
                E FAWCETT J/AU
L150           4 S E3,E7
                E HEALTHPART/PA
L151           1 S E4,E5
L152           1 S L149,L150 AND L151
                E A61K031-66/IC,ICM,ICS
L153        2927 S E3-E20
                E A61K031-706/IC,ICM,ICS
L154         150 S E3-E7
L155         319 S E18-E20
L156          54 S E24-E26
                E A61K031-7105/IC,ICM,ICS
L157         225 S E3-E5
L158       13743 S (B05-B01G OR B05-B01J OR B05-B01P OR C05-B01G OR B05-B01J OR
L159       15870 S L153-L158
L160        6475 S (?PYROPHOSPH? OR ?PYRO PHOSPH?)/BIX
L161       22154 S L159,L160
L162           3 S L149-L151 AND L161
L163           3 S L152,L162
L164         389 S L161 AND ?ALZHEIM?/BIX
L165         383 S L161 AND (B14-J01A4 OR C14-J01A4 OR B12-G04A OR C12-G04A)/MC
L166         251 S P444/M0,M1,M2,M3,M4,M5,M6 AND L161
L167         574 S L164-L166
L168          27 S L167 AND L160
                SEL DN AN 14
L169           1 S E1-E2
L170         545 S L167 NOT L163,L168-L169
L171         223 S L170 AND L153
L172          57 S L171 AND (ALZHEIM? OR AMYLO?)/TI
L173         103 S ((B115 OR B415 OR B515 OR B615)(S)(B702 OR B713))/M0,M1,M2,M3
L174          25 S L172 AND L173
L175          32 S L172 NOT L174
L176          78 S L173 NOT L174,L175
L177          88 S L171 NOT L172-L176
L178           3 S L163,L169 AND L149-L177
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FILE 'WPIX' ENTERED AT 10:18:01 ON 04 JUN 2003

FILE 'DPCI' ENTERED AT 10:18:15 ON 04 JUN 2003

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            E WO2001082932/PN
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